

Carter's nuclear moves

THIS week, President Carter is set to unveil his much heralded and extensively leaked energy policy. He has been warning for weeks that its emphasis on conservation and its moves to increase energy prices will be politically unpopular, a fact vividly confirmed last weekend when, even before the policy was officially released, it came under attack in three separate television interviews given by Senator William Proxmire, the consumer advocate Ralph Nader and the Republican National Committee Chairman William Brock—people whose political philosophies span a wide spectrum.

Clearly, it will be a severe test of the fledgling Administration's political skills to push the energy proposals through a Congress which is all too aware that soaring energy prices may swiftly translate into plunging electoral votes. Nevertheless, Carter has suggested that he is willing to try, even at the expense of a few percentage points in his popularity rating.

While Carter's domestic energy proposals are running into heavy fire at home, his efforts to curb nuclear proliferation have been attracting equally fierce and often self-interested attacks abroad. The non-proliferation proposals, announced in advance of the other energy proposals, have been criticised unofficially by some West European governments who grumble that the United States may be trying to keep them out of a lucrative business in which they have a technological lead. And it has been attacked in some developing nations as an attempt by the United States to maintain the gap between rich and poor.

First, it is important to understand just what Carter did and did not say. There was nothing very surprising in his announcement, for Carter had signalled his punch months ago during campaign speeches and in some previous Presidential pronouncements. It was not a comprehensive, detailed discussion of major proposals. Instead, Carter simply stated several policy options which his Administration intends to pursue. They are:

- The United States will defer indefinitely the commercial reprocessing of fuel from power reactors and the recycling of plutonium. This means that no federal aid will be supplied to start up a reprocessing plant built by private industry in South Carolina, and that plant may well be mothballed before it even starts operating.
- The liquid metal fast breeder programme, which has previously enjoyed pride of place as the highest priority energy research and development programme in the United States, will be scaled down and restructured to give more emphasis to research and less to development of demonstration reactors. The programme will not be scrapped, however.

- More funds will be put into research on alternative nuclear fuel cycles, such as the thorium cycle, which may pose less risk of proliferation.

- The United States will increase its production capacity for enriched uranium in order to provide assurances to countries which agree not to develop nuclear weapons of adequate fuel supplies well into the future, the objective being to try to dissuade other nations from building their own enrichment and reprocessing plants to ensure their fuel supplies.

- The United States will continue to embargo export of equipment or technology that would permit enrichment or reprocessing by non-nuclear weapons states.

- Discussions with both nuclear exporters and importers will continue, and the United States is willing to explore various arrangements aimed at developing international fuel cycle facilities and access to spent fuel storage facilities for countries sharing non-proliferation objectives.

The only new policies announced are the renunciation of domestic reprocessing by the United States and the sharp reduction in efforts on the breeder reactor programme, both of which are important precursors to international non-proliferation talks. The proposal to defer domestic reprocessing was strongly urged recently by a committee established by the Ford Foundation, whose report seems to have provided the basis of Carter's policy. The reasoning, which is persuasive, is that if the United States pursues domestic reprocessing while trying to dissuade others from doing so, it would be accused of setting a double standard and its credibility would be destroyed. Moreover, since the United States has relatively large coal and uranium resources, the incentive to reprocess is small, at best.

Carter quickly acknowledged that other industrial countries might see their own domestic programmes in a different light, since their future energy supplies might not be so stable as those of the United States. Nevertheless, the onus is now on those countries which intend to reprocess to discuss publicly the reasons which compel them to push ahead at the possible expense of some lessening of control over proliferation.

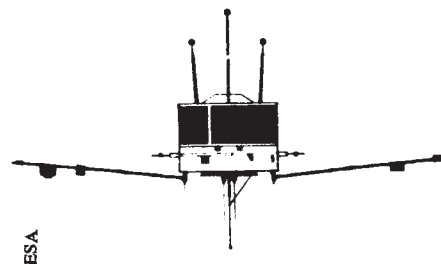
The next opportunity to discuss these matters in an international forum will be at the secret talks between nuclear suppliers which are due to resume in London in the next few weeks. Carter's statement, released a month before the talks are scheduled to resume, has set the stage for the talks and it has provided plenty of opportunity for a more thoughtful response by European governments than the mostly self-serving reactions which have been voiced unofficially so far. □



Geos

Europe's satellite for science

Geos, the ESA's purely scientific satellite, is launched this week. **Stuart Sharrock**, now in Florida, reports



THE EARTH lies inside a leaky magnetic bottle which is formed by magnetic field lines linked to the earth. Called the magnetosphere, it stops the blast of particles from the sun penetrating to the ground and prevents the escape of ionised particles from the upper atmosphere. Occasionally leaks occur, producing aurora and terrestrial magnetic storms that play havoc with radio communication and electrical power distribution. But more significant is the role the magnetosphere plays in controlling the earth's climate. Solar-climate correlations are well established and although it is clear that the magnetosphere mediates between the solar wind and the atmosphere, the exact mechanisms by which it does so are not understood in spite of the several hundred satellite missions already flown.

Study of the magnetosphere is clearly important, for it should lead to an understanding of the environment which will bring economic benefits; but there are other reasons for investigating its properties. Ninety nine per cent. of all matter in the universe is in a plasma state interacting with a magnetic field and the process by which magnetic field energy is transferred to ionised particles is of fundamental significance. This process occurs in the magnetosphere, which is therefore a unique laboratory—a private universe in our own backyard—in which we can study small-scale versions of the fundamental mechanisms that govern the behaviour of matter in the universe. Potential prizes from probing the magnetosphere range from more accurate weather predictions to a better knowledge of the nature of pulsars; from an understanding of aurora to improved prospects for controlled nuclear fusion. The basic structure and processes of the magnetosphere have now been identified and an attack has been launched on the detailed mechanisms and the dynamics of the system as a whole. It is known as the International Magnetospheric Study (IMS) and will run from 1976–79.

Two major satellite missions are at the heart of the IMS: the world's first purely scientific geostationary satellite, ESA's Geos, and a combined NASA/ESA venture comprising three satellites code-named ISEE (International Sun

Earth Explorer). Geos is scheduled to be launched on 20 April and ISEE on 14 October; as the centrepiece of the IMS, Geos has been designated the reference spacecraft for the study and will coordinate with ground-based, balloon, aircraft and rocket programmes.

The magnetosphere

A solar wind of protons and electrons blows continuously through the solar system at some 400 km s^{-1} and, according to Alfvén's 'frozen-in' theorem, drags with it the Sun's magnetic field. The earth's dipolar magnetic field and the ionospheric plasma are similarly frozen together. These two magnetic fields cannot mix and so the earth's field lies in a closed cavity in the plasma stream from the Sun and presents a tiny obstacle to the blast of the solar wind. This magnetic bubble is the magnetosphere; it is deformed from a dipolar configuration by the solar wind and the size of the magnetospheric cavity changes in response to the strength of the wind. At typically 10 earth radii the hot plasma from the Sun is deflected and streams around the earth's protecting magnetic bottle; under certain conditions however the bottle becomes open to the solar wind—with drastic consequences. Within the magnetosphere there are numerous plasma regions which respond to changes in the solar wind and which interact with the ionosphere and the atmosphere.

Observations with a single satellite can never distinguish unambiguously between spatial and temporal variations; two satellites orbiting together with a known separation are needed and this is one of the aims of the ISEE mission. Geos will sample the different regions of the magnetosphere, measure minute variations in all the particle and wave parameters without interference from the satellite itself, monitor conditions continuously over many months, and yet be capable of responding to changing situations in minutes, and explore the coupling between the magnetosphere and the ionosphere by enabling correlated satellite and ground-based measurements. These requirements specify a satellite with an orbit, construction and performance an order of magni-

tude more complex and sophisticated than any previous ESA satellite and with a control and ground support system more ambitious than has so far been attempted by NASA with unmanned missions.

The Geos satellite

Built by a consortium of European industrial contractors headed by the British Aircraft Corporation, Bristol, England, Geos will be placed into a geostationary orbit 36,000 km above the equator. The orbit covers a region of the magnetosphere where many of the dynamic processes responsible for magnetic and ionospheric disturbances are believed to develop; the satellite will be positioned at longitudes where the magnetic field lines are conjugated to both auroral zones (that is, particles passing along the field lines through the satellite will arrive at the aurora), allowing correlated measurements to be made from ground stations and rocket-borne instruments.

As the spatial variations seen by Geos will be small, the time and space ambiguities will be minimal and short-lived transient phenomena can be studied. Sampling of different regions of the magnetosphere will be automatic as Geos alternates between the day-side and the night-side, but the boundaries of the different magnetospheric regions are not fixed in space and will at times move across the geostationary orbit under the influence of the solar wind; phenomena associated with such boundary crossings are of particular interest.

Once in orbit, Geos will be permanently in view of a purpose-built tracking and data recovery ground station near Darmstadt in West Germany (also to be used for Meteosat). The continuous link between the satellite and the ground allows for high data rates, which are essential for some experiments, and means that real time modification of experiments becomes possible. The capability of closed loop control of instrument modes is crucial and was laid down as a ground rule for the mission in the early planning stages.

The problem with many satellite experiments is that effects caused by the spacecraft itself can often mask or destroy the phenomena of interest. Spacecraft charging is well known—

potentials of up to 10 kV have been reported from the ATS satellites during eclipses—and can have disastrous effects on experiments to measure low energy particle fluxes. To minimise this problem the whole of the outer skin of Geos has been made conducting, thus ensuring that the surface is an equipotential. There is a complex system of eight booms which deploy in orbit to take the sensitive detectors up to 20 m away from the disturbing influence of the satellite body; this is the most complex boom system attempted for any European satellite. The experiments mounted on Geos involve extremely sensitive measurements (for example the detection of magnetic variations of a thousand millionth of the strength of the earth's magnetic field) and this has meant an extensive programme to minimise electromagnetic interference caused by equipment on the spacecraft.

The experiments

The achievement of providing a magnetospheric laboratory free from interference, accessible in real time and controllable from the ground is matched by the scope of the experiments comprising the payload. To understand the magnetosphere's structure and the wave-particle interactions that occur, it is essential to make sensitive measurements of all relevant parameters simultaneously. For the first time this is being done and data on every quantity of interest are being collected: four experiments will measure particle fluxes and their variation with energy and direction, covering a range from thermal energies to hundreds of keV, and three experiments will measure electromagnetic waves over a frequency range 0–77 kHz for electric fields and 0–20 kHz for magnetic fields. DC electric and magnetic fields will be monitored with extreme sensitivity. The most important measurements will be duplicated by independent experiments.

A mission this complex cannot hope to satisfy all the requirements of a number of coordinated campaigns; many of the needs are mutually exclusive and inevitably compromises must be made. The coordination of activities is crucial to the success of the mission and has been an important factor in its planning. Areas in which the standard configuration is not ideal can hopefully be covered by special arrangements; the project has the inherent flexibility to allow this.

As an example, a polar expedition to a ground station in the Arctic could be unhappy about the orientation of Geos. The expedition will want to correlate its measurements with particle fluxes coming from the south at the

position of Geos but this is only possible during the northern winter. The directional coverage for particles is not isotropic and the orientation of Geos is governed by the requirement that the radial booms do not shadow the solar cells. Inversion of the satellite—a delicate operation—would have to be arranged but it would interfere with the wave experiments and expeditions to the Antarctic would not be too happy. Other ground stations would no doubt have conflicting requirements. Rocket campaigns, for example, are costly and can only be conducted at certain times, and these are sure to be the times when interesting transient effects are manifesting themselves and necessitating an immediate change in plan. In any case there is only a limited supply of fuel so manoeuvres are rationed. The coordinating committee will have a tough time but the number of demands made on the mission is a measure of its flexibility and importance; the number of satisfied customers is likely to be very high. Crucial to this flexibility is the provision of extensive computing facilities at the ground station where the data are collected.

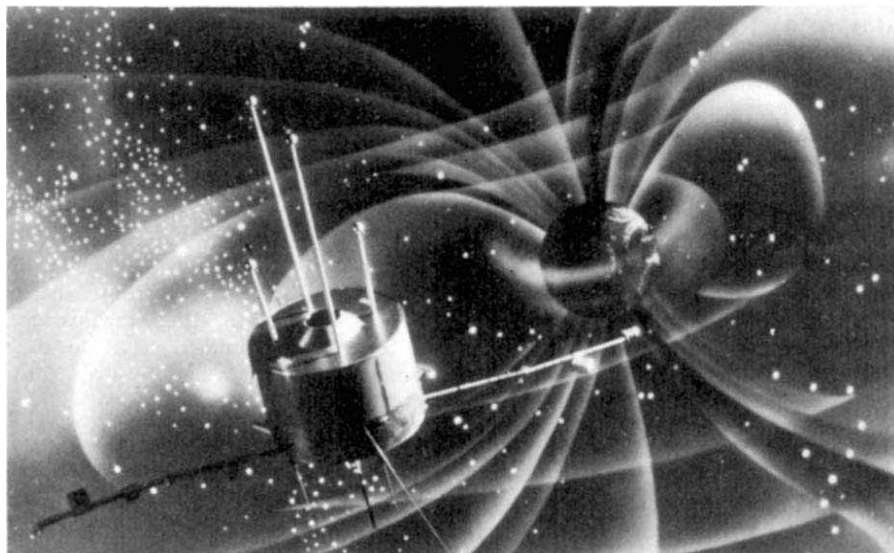
Coping with data

Most of the time nothing exciting will happen (the magnetosphere can remain stable for long periods) and it is unwise to accumulate vast quantities of data throughout the mission. Filling a magnetic tape every 45 minutes, Geos would generate 26,000 tapes over a two year period of which only about 10% would be worth keeping. The solution is to recycle the magnetic tapes every three months; there is an extensive data distribution system (it includes daily summaries of all Geos data) to enable a communal decision on which data are to be retained. Not only does Geos have the ability to respond

quickly to changes in the magnetospheric system, it also imposes a requirement on the experimenters to respond to their data within a reasonable time period—a valuable constraint that could be more widely adopted.

Originally planned for August 1976, the launch of Geos has been delayed until April 1977 mainly because of late delivery of components. The satellite will be launched by a NASA Delta launch vehicle from the Kennedy Space Center in Florida. The original flight plan has been continually modified to take account of the magnetic conjugacies between a given longitudinal position of the satellite and the positions of available ground stations and rocket campaigns. The current plan is to station it initially at a longitude of 0°, where a double magnetic conjugacy exists between Iceland in the northern hemisphere and the Syowa base in the southern hemisphere. In about August this year Geos will be drifted eastwards to arrive at about 35° E by October 1977; this is a position ideally suited for correlated measurements with the extensive array of ground-based stations and rocket ranges in Northern Scandinavia. In mid-1978 the satellite could be thrust back to the 0° position again, further movements being a function of the status of polar expeditions, rocket campaigns, ground stations, the amount of fuel remaining, the consensus of opinion and the tempers of the Coordinating Committee.

After lift-off it will take about a month to get Geos into its correct orbit with the extensive boom system correctly deployed, another month to check out the experimental payload; by then hopefully it will be fully operational and the IMS can start in earnest. The taxpayers of Europe have made a wise investment in Geos—if NASA gets it up there. □



An artist's impression of Geos in the magnetosphere

A partial triumph

Vera Rich assesses the Moscow Seminar, which celebrates its fifth anniversary this month

THE illicit Moscow 'Sunday Seminar' for *refusnik* scientists was founded five years ago this month. In a remarkable development after such a lengthy period of harassment of its organisers and participants, the Soviet authorities have now informed Professor Mark Azbel, the current leader of the seminar, that he may hold a special anniversary meeting this week provided it is confined to matters of strictly scientific interest.

The first Sunday seminar for *refusnik* scientists—that is, Jewish scientists dismissed from their posts and deprived of all official means of pursuing their careers—took place in Moscow on 12 April 1972. The date is significant—1972 was the year of the 'education tax', by which any Jew wishing to emigrate to Israel was obliged to repay to the government the 'cost' of any higher education he may have received. And since such education is provided *gratis* by the State, the authorities could clearly fix its notional cost at any value they chose.

Scientists wishing to emigrate became liable to long waiting periods between applying for a visa and receiving permission to emigrate. They therefore began to form one of the most significant social groups within the growing class of *otkazniki* (the word which later became transformed in English to 'refusnik')—those not permitted to leave the country, yet deprived of their professional means of livelihood within it.

Moscow meeting

Against this background, a modest group of 17 scientists met in the Moscow flat of Dr Henrikh Sokolnik in April 1972. The venue was chosen because Dr Sokolnik is a chair-bound cripple. Their aim was to read papers of mutual interest and thus to keep up the interplay of ideas without which scientists cannot function professionally. Throughout 1972 the group functioned quietly without attracting the attention either of the Soviet authorities or of Western sympathisers. Even the weekly *Bulletin Jews in the USSR*, founded that year to publicise the plight of *refusniks* and Jewish prisoners of conscience, made no mention of the seminar, although it carried numerous appeals from scientists to their colleagues abroad, and news items about scientists suffering particular hardship (notably Dr Evgenii Levich, who in that year was

sent to a Siberian labour camp).

It was not until 1973 that the first information about the seminar began to reach the outside world. In that summer, when an International Conference on Magnetism was meeting in Moscow, several Western scientists, learning of the exclusion of the *refusniks* from the conference, made their way to the flat of Professor Aleksandr Voronel, where the seminar was then meeting, and took part in a lively and informative discussion. From this contact the idea arose of holding an International Session of the seminar the following summer.

The International Session was widely announced. In addition to Professor Voronel, two organising secretaries, Dr Norman Chigier of the University of Sheffield and Dr Edward Stern of the University of Washington, Seattle, were appointed. Papers were invited on an international basis, and more than 50 leading scientists, including seven Nobel prize-winners, lent their names, either as patrons or as would-be contributors. The preparations caused considerable disquiet to the Soviet authorities which, in the stress of the situation, made what can be seen in retrospect as a tactical mistake.

Had the seminar been permitted to take place, then coming as it did at the height of the scientific conference season (July) and virtually coinciding with President Nixon's visit to Washington, it might have merited at best a paragraph in the foreign press as a promising sign of a new 'thaw'. Instead, prospective Western visitors were denied entry visas, the proposed venue was put under KGB supervision, the Moscow organisers were arrested and taken to detention centres outside the city, and other would-be participants were kept under virtual house arrest. The 'Seminar-that-never-was' accordingly went into history as a major example of State interference in academic freedom, and the 'Voronel Sunday Seminar' became an important (if unofficial) item on the schedule of scientists visiting Moscow in the course of their professional duties. It is estimated that, to date, some 150–200 foreign visitors have attended the Seminar.

Remarkable survival

The survival of the seminar over five years is, under Soviet conditions, remarkable. Of all those who took part in the first meeting only one is

still in Moscow: Corresponding-Academician Veniamin Levich. The others, one by one, and largely due to pressure from their Western colleagues, have received their permission to leave. Professor Voronel himself received an exit visa some six months after the non-occurrence of the International Session, and his role as leader has been inherited by Dr Mark Azbel, with, in recent months, Dr Anatolii Shcharanskii acting as press attaché and contact with the international scientific community.

As the more 'senior' members of the group leave, there are always new *refusniks* to fill their places, and there seems little likelihood that the need for a seminar will disappear within the foreseeable future. Indeed, the seminar movement has proliferated: by last summer some ten additional seminars had been established dealing with specialised topics, including theoretical physics, computer science, radio-electronics, and biology; and one seminar, in Kiev, after being officially 'closed' by the KGB, began meeting in a public park. Organisers and participants from all groups have experienced constant harassment including police interrogation, confiscation of books and papers, and short-term arrests.

One reason for the Moscow Seminar's survival is undoubtedly the interest shown by many scientists abroad. For them, the existence of a clear-cut ethical issue is involved: the UN Declaration on Human Rights states unequivocally that everyone has the right to leave any country, including his own. But in practice a number of caveats arise as far as scientists are concerned which makes the right difficult to exercise. Access to classified information is one objection; another, which in the case of the Soviet Union gave rise to the notorious 'education tax', is the brain drain with all its attendant questions of how far a student, in accepting a place for higher education, may be deemed to have implicitly entered into a contractual obligation to work in the country which has financed him.

Scientists remain shocked, however, at the idea of their colleagues being prevented from functioning as scientists. The holding of seminars and discussions, access to new publications and correspondence and meetings with foreign colleagues, all constitute a major part of the scientist's basic activity. Even if the Soviet authorities see fit to dismiss from their professional posts scientists so 'disloyal' as to wish to emigrate, and to restrain that emigration in the interests of the State, it seems illogical then to prevent them exercising, even unofficially, that pro-

fession which makes them a State asset. The right of the refuseniks to hold seminars must appear unequivocal, even to those of their foreign colleagues who are disinclined to enter into long arguments against the Soviet government's pragmatic case for denying exit visas.

Contribution not great

But what, scientifically, is the value of these seminars? From the point of view of the progress of world science, it must be admitted that the Soviet contribution is not great. A handful of papers by refuseniks has been accepted by foreign journals, but it is significant that these are by the more mature members of the group—notably Veniamin Fain, Mark Azbel and Viktor and Irina Brailovskii. The papers are, presumably, the working-up of ideas which the authors had no time to develop during their active careers, and for young scientists, who have not yet developed such a back-log of topics, the prospect of publication abroad is probably somewhat bleak.

Nevertheless, from the point of view of the scientists themselves, attendance at the seminar is something more than a holding operation. Soviet science, aimed as it is at serving the national economy, can be extremely narrow, so that one hears of first degrees in such topics as light metal engineering for the civil aviation industry. Moreover, theoretically Soviet science must serve socialism, and every working scientist must, officially at least, formally confirm his political commitment.

In the Seminar all this is changed. Thrown out of their jobs, the refuseniks found a new freedom in their release from this tacit agreement to serve political ends. "We stopped mourning for our scientific interests, since, in truth, we had attained the ideal of scientific detachment", Voronel explains in his preface to the 'Proceedings' of the Seminar-that-never-was. At the very first meeting, Levich joked that "This reminds me of my youth. Back in a group of Jews again, and once again they talk nothing but science".

Over the years, this first flush of euphoria has somewhat faded, but the broadening of the participants' interests has not. Asked last week to comment on the achievements of the Seminar during its five years' existence, Professor Voronel remarked:

"The main difficulty of the seminar has been to combine the different interests of its participants, but it can also be an advantage because they become aware of different fields. This may be of great value to contemporary science, to have such an interdisciplinary forum."

He cited the case of Shepelev, who from a discussion of general principles of phase transitions developed a new approach to his own subject—the strength of rubber and polymers. He also spoke of Roginskii, originally a nuclear physicist, who during the course of the seminars became interested in solid state physics and, on receiving his visa, was able to take up a post at the Hebrew University, Jerusalem, working in this new field.

This broadening of intellectual interests is, of course, considerably restricted by the lack of access to published literature, particularly from abroad. One project in particular, a sociological study for which surveys and questionnaires were distributed under conditions of great difficulty, would have had considerably greater intrinsic value had comparable figures, published during the past few years in the USA, been available for comparison. Foreign scientists have been invaluable as a source of information on the main trends of research abroad, as well as a profound source of moral support.

How much easier?

The fact that the authorities have given permission to hold the one meeting (although, strictly speaking, no such permission is required, since the Soviet constitution guarantees the right of assembly) will not necessarily mean that there will be no interference with the regular Sunday meetings. And, even if these can proceed without harassment, access to published literature will still be restricted to those few members who have retained their right of entry to academic libraries, and to the few hand-written copies of the primary journals available as *samizdat*. Experimental facilities will be lacking, and although the Russian term *nauka* covers the humanities and social sciences as well as the physical sciences, it seems unlikely that the authorities would look with favour on any further attempts to make sociological surveys; the data from the first such survey was confiscated last December.

Any attempts to hold another International Session, as opposed to welcoming visitors on an *ad hoc* basis, would doubtless still be interpreted as a 'foreign provocation', as it was in 1974. Furthermore, Anatolii Shcharanskii, the Seminar 'spokesman', is still in custody, facing the possibility of treason charges being brought against him; and within the past few months several members of the Seminar have been accused in *Izvestiya* of being agents of the CIA. Even if permission were now to be extended to the regular meetings of the Seminar, this would



Azbel (top) and Voronel: activists

be of little value if it were to be accompanied by harassment of individual participants on grounds other than their membership.

The granting of the permission is nonetheless of far wider significance than a grudging acquiescence in the holding of a one-off celebration. Just as, in the words of Professor John Ziman, the true value of the Seminar "is not the work they are doing but the fact that they are doing it", so too the significance of this permission is not that the Soviet authorities will permit one special meeting of the Seminar to be held, but the fact that they admit the Seminar exists at all. In 1974 foreign scientists wishing to attend the International Session were refused visas on the grounds that they had not been invited by a *bona fide* organisation. In December 1976, when the Seminar group was to hold a special symposium on Jewish life in the USSR, the leaders were arrested and their right to hold the symposium was emphatically denied. Throughout the past five years, the authorities have done their best to deny the existence of the Seminar, and proceedings against its members and activists have been brought on other counts, such as 'parasitism' (being without visible means of support) or 'slandering the State'. The granting of permission even for one meeting represents a real achievement, not least for science. □

USA

Geophysics stakes its claim

A draft report proposing a massive deep sea research programme is now circulating among US earth scientists. Colin Norman reports from Washington

A PROPOSAL for an ambitious deep sea research programme, costing some \$400 million over the next decade, is being put together by a group of earth scientists and will soon be forwarded to the National Science Foundation (NSF) for further study and possible funding. The proposal, based largely on recommendations developed during an international meeting held last month at Woods Hole, Massachusetts, would involve extensive drilling deep into the ocean floor in regions which have not yet been punctured by research probes.

A central feature of the proposal is to convert the infamous *Glomar Explorer*, the vessel used by the Central Intelligence Agency in 1974 to scoop bits of a sunken Soviet submarine from the bottom of the Pacific, into a sophisticated drilling ship. The *Explorer*, which is now in mothballs near San Francisco awaiting a user, would be capable of drilling at depths and in regions which are beyond the reach of present drilling vessels.

Though it is far from certain that the proposal will be funded, at least in its present form, it is sure to attract considerable attention as it wends its way through the federal bureaucracy. And the attention will not be confined to the United States, for NSF is expected to seek international participation in the venture if it decides to apply to Congress for funds.

A draft report outlining the proposal is now being circulated among a number of earth scientists, and a copy has been made available to *Nature*. The proposal would involve a major expansion and re-direction of the Deep Sea Drilling Project (DSDP), a programme begun in 1968 which has resulted in the drilling of more than four hundred holes in the ocean floor in many parts of the world. DSDP now runs an international effort called IPOD1—the International Phase of Ocean Drilling—which is supported by six different countries (the United States, which provides the bulk of the funds, France, Germany, Japan, the USSR and the UK). It has helped to revolutionise thinking about the history of the earth, but after several extensions it is due to expire in September 1979.

The new proposal is thus an attempt to map out a research effort to carry

on where IPOD1 is expected to leave off. Drafted by an international committee headed by Manik Talwani of the Lamont-Doherty Geological Observatory, the proposal is the result of an elaborate planning effort involving scores of earth scientists. The committee was established last August by the executive council of JOIDES (Joint Oceanographic Institutes for Deep Earth Sampling)—a collection of research institutes which are taking part in the DSDP—and it was given a broad mandate to plan a research effort stretching over the next decade.

The committee's proposals are based on a series of 'white papers' drawn up by groups of scientists and discussed at the Woods Hole meeting last month. Its report has been approved in principle by the JOIDES executive council, and it is now in the final stages of revision before being published.

The DSDP has already provided masses of information confirming and refining the theory of plate tectonics, according to which the continents were once joined together in larger land-masses which were split apart by processes which still push the continents around. Those processes, known as sea floor spreading, involve the continual generation of new oceanic crust along the mid-ocean ridges where molten lava wells up from the mantle, solidifies and is pushed aside by yet newer lava. This constant generation of new crust gradually forces continents apart and is responsible for a variety of geophysical and geological phenomena, such as earthquakes, volcanoes, and large scale uplift of mineral deposits in many regions where oceanic and continental crusts converge.

Though rock samples recovered from many parts of the world by the DSDP drilling vessel, the *Glomar Challenger*, have produced solid evidence in support of the plate tectonic model, a number of intriguing questions remain (see also *Nature*, 259, 83). They include a satisfactory explanation of why the continents split apart when they did, a better understanding of the active processes taking place along the oceanic-continental margins and an appreciation of the large-scale climatic and oceanographic changes which have accompanied the formation and evolution of the oceans. Many of those questions could only be answered by drilling into the ocean floor in regions which are at present inaccessible to the *Glomar Challenger*.

In particular, some of the most intriguing drill sites lie along the continental margins in regions where

there is a risk of encountering oil and gas deposits, or deep in the ocean trenches where very long drill strings would be required, and at high latitudes where rough seas and ice present problems. A ship capable of coping with those conditions would require massive lifting capacity to handle the heavy equipment needed to prevent blowouts of oil and gas and to operate long drill strings. It would also require powerful engines, a thick hull and good station-keeping ability to work at high latitudes. Such a vessel would cost about \$100 million to build, according to NSF estimates, a price tag which probably puts it out of reach. That, however, is where *Glomar Explorer* may come in.

Built for the CIA by Global Marine Inc., the same company which owns and operates the *Glomar Challenger*, the *Explorer* has been idle since 1975 when its mission became publicly known. Though it belongs officially to the federal government, a number of attempts to find a user for the vessel have so far drawn a blank. Last year, however, NSF expressed interest and commissioned Global Marine to study the feasibility of converting the ship into a deep sea drilling vessel. The study, which has recently been completed, concludes that it would cost about \$52 million to convert the *Explorer* into a sophisticated drilling vessel, equipped with a riser to prevent blowouts if oil and gas are struck. The cost of operating such a vessel would be about \$33,000 per day, about twice that of the *Glomar Challenger*. In other words, the *Explorer* could provide a cutprice entry into the more intriguing drill sites, and the Talwani committee envisages it becoming the principal actor in a deep sea research programme in the late 1980s.

The proposed programme would essentially involve continuing use of the *Glomar Challenger* to drill relatively shallow boreholes in accessible sites until October 1984. In the meantime, the *Explorer* would be converted in time to start drilling in 1981. It is anticipated that the programme would run until October 1987, and the total cost, including preliminary surveys and sample analysis but excluding the cost of converting the *Explorer*, would be about \$396 million.

The proposed effort would include drilling in the passive margins—the continental margins which originally fitted together—in an effort to understand the processes which led to the original fusion of the super-continent. Another major thrust would be to drill along the active margins where the Earth's crust is being jostled and subsumed into the mantle, in an attempt to understand some of the geophysical

processes involved. Other features of the proposal involve extensive drilling into the ocean crust itself in an effort to learn more about the processes by which it was formed, and to study the evolution and environmental changes which have occurred.

The committee cautions that the programme should not be attempted at all unless there is a firm assurance of support for extensive geophysical survey work before drilling takes place, and sufficient funds to analyse and interpret the results. "An investment in a drilling vessel without a commensurate investment in scientific investigations on an appropriate scale could not be supported in good conscience", the report states.

The proposal will be sent officially to NSF in the next few weeks, and responsible programme officials will seek authority from the Director and the National Science Board to look further into the scientific merits of the plan (a task which, as one NSF official wryly observed last week, will be complicated by the fact that virtually everybody capable of offering an independent opinion participated in drafting the proposal). If the programme is deemed meritorious, NSF will eventually seek funding, first from the Office of Management and Budget and later from Congress. At some stage, it is almost certain that the matter will land on the desk of Frank Press, President Carter's science adviser, who is a distinguished geophysicist himself.

For a project of that cost and scope, international participation would be an obvious advantage. At present, non-US participants in the DSDP each contribute \$1 million a year in direct costs and a further sum in supporting the work of their own researchers in analysing and interpreting the results. NSF officials note that economic and political difficulties might mitigate against foreign participation.

The British commitment, for instance, is to support IPODI until 1978, and a request for a further year's support is expected soon. The British package of support is complex, however, involving sums of money from three separate departments, and any request for financial commitment at this stage for a period of ten years might pose problems.

The first decade of drilling with the *Glomar Challenger* has provided some spectacular results and answered some fundamental problems. But it has also thrown out some intriguing questions which can be answered only with more expensive equipment which will be more costly to operate. The same pattern can be discerned in fields such as particle physics and even molecular biology. It should be no surprise that it is now happening to geophysics. □

NETHERLANDS

Dutch go ahead on DNA

Casper Schuurings reports from the Netherlands on moves to control recombinant DNA research there

RECOMBINANT DNA research should be developed in the Netherlands because of its great scientific importance, according to a report from the country's Commission on Genetic Engineering which was handed over to the Ministers of Health and for Science Policy on 3 March and published on 30 March. The research should be carried out with stringent precautions and according to clear regulations contained in legislation which, in the commission's opinion, should be implemented quickly.

The commission, which started work just one year ago, also proposes a special committee with responsibility for surveillance of the research. It would continue the work of the present commission on a legal basis, and have on it representatives of the biomedical sciences, of other related sciences (legal and ethics), of the government and of society at large. The commission, which consists only of experts in the field, also suggests another committee to consider broader ethical and social aspects of the applications of advanced medical and biological research and whether to bring such research within the framework of legislation.

The commission supports the European Science Foundation's recommendation that the rules of the British Williams report be followed, but considers that on a couple of points the report is insufficiently clear. Plans for recombinant DNA research must be reported to the 'surveillance committee', and research cannot go ahead unless a statement that there is no objection to it has been obtained and an 'examination commission' has been established to check that all requirements are fulfilled. That body has the right to do investigations on the spot.

The commission prefers the description of the four levels of physical containment of the Williams report. It says that a laboratory with the highest containment level should not be established in the Netherlands, and that experiments on that level should be done at a 'European' laboratory, but it says there is a great need for facilities with containment one level lower. Regarding levels of biological containment, the commission has opted for the rules contained in the NIH regulations in the USA. For each experiment the requirements for biological containment will be left to the surveillance committee.

The commission also prefers the NIH view that certain experiments should

not be carried out at the moment. The Williams report did not exclude any experiments completely. Those prohibited include the cloning of recombinant DNA from pathogenic organisms (class 3, 4 and 5) or from oncogenic viruses; the purposeful cloning of that DNA from organisms coding for the production of toxins (botulinum, diphtheriae); the establishment of a transfer of resistance against (for example) antibiotics to microorganisms missing that natural resistance; and experiments enhancing the virulence of phytopathogenic microorganisms.

On a list of examples of experiments with non-purified DNA of organisms not secreting toxic products and the conditions under which they should be carried out, the commission separates primates from other mammals, which the Williams report did not do. Concerning prokaryotes the commission distinguishes DNA from organisms which exchange genetic information with *E. coli* and those which do not. In the commission's opinion the second category carries a higher potential risk. Finally, experiments which use nucleic acid from animal viruses not pathogenic for man have to be placed in a higher category than the Williams report suggested.

So far nine projects, one of which is already in progress, have been lodged with the commission. One has to be classified as belonging to the category of research which cannot be carried out in the Netherlands; the level of two others has not been determined, while another two are P1-level experiments and two more are P2 (according to NIH regulations). Two others are P1 projects.

The establishments involved so far are the University of Amsterdam (3 projects), the Free University in Amsterdam (1), the University of Leiden (3), the University of Groningen (1) and the University of Nijmegen (1). Other universities and research institutes are preparing to do recombinant DNA research. From industry only Unilever is making preparations.

The foundation 'Biosciences and Society', which gives information on a regular basis on biomedical subjects, remarked on the report in its 31 March bulletin. It says that the commission, "consisting exclusively of prominent Dutch scientists, has hardly occupied itself with the social desirability of the recombinant DNA-research". It goes on: "The report gives no answer to the critics who doubt whether this research is socially necessary. These critics say that some results can also be reached another way." □

EUROPE

Wanted: a science policy

Chris Sherwell reports on a European science policy symposium held in Brussels last week

STRAITENED economic circumstances concentrate the minds of policy-makers wonderfully. The problems of those involved in science policy are worse than most, however, for the additional reason that, with science seemingly everywhere, science policy is seemingly nowhere. But with the research base an important pillar of support for the developed countries' economies, the need for science advice in government rightly remains undisputed, and the need to deal with problems with a scientific content is undiminished. So the search goes on.

As part of that search, the European Commission last week sponsored a three-day symposium at a fashionable hotel in Brussels. Ambitiously entitled "Strategies for Europe: Proposals for science and technology policies", it was organised by the private grouping known as the Science Policy Foundation, and attended by some sixty people drawn from research councils, research institutes, universities, industry and the media as well as governments.

It may remain the most important outcome of the meeting that the lines of thinking developed in recent years under the inspiration of the 'Europe + 30' idea are at least being supplemented and that concern has begun to focus on more immediate problems. If so the involvement of the Science Policy Foundation could increase, although notable absentees from the meeting, particularly from Britain's science policy establishment, may mean that any transfer of legitimacy will take time. A former Director General at the Commission, Michael Shanks, suggested in drawing conclusions from the meeting that there ought to be an organisation of science policy federations whose work could be enriched through association without being subordinate to it, and that this possibility ought to be examined, perhaps by the Commission working with the Science Policy Foundation. There was a need, he said, for the Community to have a loose network of experts independent of political allegiances who could together provide advice on common problems for leaders lacking a science education and thus help to bridge the gap between them and the broad community they served.

To this end Directorate General

XII, the department of the Commission which with its responsibilities for research, science and education provided the crucial support for last week's symposium, is now engaged in preparing for two events. One is a three-day symposium which it is organising for June on the issues which the phrase "Science and Society" now commonly embraces. It is understood that this has met with resistance from some scientists and policy makers in certain member countries but has been welcomed by others. The Commission's view is guarded, but it appears prepared to see the issues given an airing under its auspices on pain of withdrawal if the experiment is as fruitless as its critics imply.

Preparations for the other event are less well finalised. It stems from the suggestion in February by Guido Brunner, the European Commissioner for both Energy and Research, of a forum or hearings on the issue of nuclear power. What form these might take remains unclear, but they are likely to be held after the proposed symposium on science and society. What is certain is that, in the aftermath of President Carter's recent announcement on nuclear power, the already strengthening worries of the Commission on the issue have been further reinforced. Faced with an increasingly threatened European nuclear programme and continuing troubles over uranium supplies from North America, the fact that Euratom and the IAEA have now agreed terms on safeguards seems to cut little ice, and this is a matter for some despair. The Carter statement confirms the difficulties of the Commission's own position: its first official response last week (the initiative will be "studied closely") was well muted.

If the symposium was anything to go by, on the science policy front it is now apparent that in Europe there is an emerging concern with two problems in particular. One is the effect of producing increasing numbers of highly qualified science graduates for whom the end of an era of university expansion has coincided with a period of inflation and recession to produce the grim spectre of unemployment. The worry is not just about where the professors of future generations will come from, or about the more fundamental matter of the state of science and research; there is also the practical worry, outside the issue of ageing research staffs, of the sheer waste involved, the opportunities foregone.

For those who choose to ignore such central matters of how much a country should devote to basic research—an issue on which researchers are more and more being called upon to defend themselves—the obvious destination for graduates is industry. But industrial innovation is the other problem over which there appears to be emerging concern in Europe: how is manufacturing industry, the so-called engine of growth, to improve its capacity to generate and harness the process and impact of innovation?

One tangible achievement of the symposium may turn out to be that it encouraged the first steps towards some amelioration of these sorts of problems. On the matter of industrial innovation, for example, in which the Commission has for some time shown an interest, for instance through its so-called Brunner-D'Avignon task force, the prospect emerged of co-operation between the Commission and the European Industrial Research Management Association (EIRMA), possibly with the additional assistance of the Science Policy Foundation.

Inevitably the Community's main interest, being borne of shared economic interest, is likely to focus more readily on innovation in this fashion. But it does not confine itself to that, and the symposium also confirmed that the European body that has firmly established itself as the one best placed to answer questions about the overall state of basic research throughout the continent is the Strasbourg-based European Science Foundation (ESF), made up of research councils and academies from 45 member countries.

The European Commission has close links with the ESF, and now plainly recognises its authority to speak on matters of basic research. A keynote address from Dr Gunter Schuster, Director General at DGXII, helped the ESF's President, Sir Brian Flowers, to draw a positive response later to his own intimations that the Commission could assist in efforts to establish a fellowship scheme to help build a European social science and to develop the humanities—a goal which reflects the ESF's own desire to concern itself less with the English *science* and more with the broader German *wissenschaft*. As Sir Brian said, the ESF was not concerned with studying policy; by its activity it contributed to it.

For most practising researchers that view will probably provide some real comfort at a time when their need is not so much for science policy studies as for science policy itself. The question remains whether they can represent this interest successfully. □

WEST GERMANY

The cost of maintenance

Werner Gries reports from Bonn on West Germany's funding for science

WEST GERMANY spent DM24,200 million on scientific research and development in 1976: DM12,700 million came from the government, DM10,900 million from industry and the remainder from overseas and from independent foundations. As is customary, 55% of the government contribution was raised by the central government, and 45% by the *Länder* which comprise the federal republic. In contrast to other Western nations, military research and development plays a comparatively minor role in West Germany: in 1976 it received DM1,500 million—6% of the total research expenditure. Since 1973 there has been no increase in the resources available for research and development and plans for 1977 show that in real terms, total expenditure on research will decrease. In 1976 2.2% of GNP was spent on scientific research.

Non-nuclear energy research is receiving increasing support from both the government and industry. The government contribution for specific projects connected with non-nuclear energy amounts to DM270 million in 1977. Some DM300 million will be spent on research centres and other projects. Mining and coal technology are the most important areas receiving government subsidy. New

techniques of searching for and developing petroleum, natural gas and uranium are also being investigated, as are the possibilities of solar and wind energy. Solar collectors for heating are now so advanced that the government is considering offering special incentives, particularly investment bonuses, to encourage manufacturers to put new techniques on the market. The government is also subsidising research into new methods of saving energy.

On the nuclear front, West Germany is, amongst other things, developing the fast breeder reactor. About 2,300 people are now employed on the development work and in 1977 about DM380 million will be made available to research establishments and industry for further development. The principal project is the 300 MW prototype reactor at Kalkar, which according to the latest estimates will cost DM2,800 million to set up. A smaller experimental reactor is being built in Karlsruhe to test the fuel elements for the fast breeder. Plans are also going ahead for the construction of larger fast breeder reactors in collaboration with France. German electricity supply companies are involved in the construction of the French Super-Phénix, for which they are receiving a grant of DM55 million from the West German government.

The Ministry of Research and Technology is in charge of all government activities in the field of fast breeder development, and although

there is growing opposition to these reactors in parliament, the Ministry apparently intends to continue promoting intensive research on them. So far the government alone has spent DM2,100 million on the development of fast breeder reactors. In addition to the prototype at Kalkar, a large fast breeder reactor is scheduled to be built in the early 1980s. Its construction will take into account the results of the French project; there has been close cooperation between France and West Germany on fast breeder development since the treaty between the two countries in 1975.

In 1977 space research will receive DM600 million almost exclusively from the government, and in particular from the Ministry of Research and Technology: DM347 million will go to the European Space Agency and form the major part of West Germany's spending on space research. At the moment the West German government is primarily involved in financing the ESA Spacelab and in the development of various exploratory satellites. It gives DM 40 million a year towards developing the launcher Ariane; an extra DM 10 million will go towards the building of a launching base for the Ariane in Kourou in French Guiana.

Support for national space projects has decreased steadily in the past few years and now only 20% of the total expenditure goes on domestic projects. In 1977 DM133 million will be spent on a large research establishment for air and space travel, Deutsche Forschung-und Versuchsanstalt für Luft und Raumfahrt (DFVLR). □

SWEDEN

A catalytic note

Wendy Barnaby reports from Stockholm on Sweden's recently established Energy Institute

SWEDEN'S new international Energy Institute, opened recently in Stockholm, is planning to carve a niche for itself in research on energy/ecology problems. It will see man's use of energy as a special case of the energy flow in the biosphere, affecting it and all natural resources. This should be a suitable focus for the new Director, Professor Gordon Goodman, a British ecologist with wide experience in energy research, and it is in line with the interests of the chairman of the international board, Professor Jack

Hollander, an American who heads a large project on energy for the US Academy of Science.

Specific research projects will depend largely on the results of the review of current energy research that Goodman and a plasma physicist, Lars Kristoferson, are about to begin—both want energy researchers to notify them of projects being done. The idea is to close those gaps created by the transdisciplinary nature, long time-scale or low economic interest of the work needed to fill them. The Institute will not therefore be interested in short-term, controversial topics; Goodman wants to establish its reputation as a trusted supplier of timely and significant facts for the international debate on energy-related problems. He

envisages the Institute playing a catalytic role by preparing review papers highlighting the need for research in various areas. As it has no laboratory facilities, its work will be carried on by seminars, symposia and publications.

The Institute's funds are very limited—about \$400,000 a year for the next seven years from the private Beijer Foundation—and additional funds will have to be sought elsewhere to get a reasonable programme going. But Goodman points out that the money has no strings attached and will enable the Institute to avoid projects meant to bolster sectarian interests. Because of the financial limitations, permanent positions will probably be limited to the Director and his assistant; academics coming to Stockholm for short visits or sabbaticals would help carry out projects. □

IN BRIEF

JET meeting

The Committee of Permanent Representatives (COREPER) in Brussels, made up of senior officials of the EEC member states, meets this week to discuss the ill-starred joint fusion project, JET. If they can resolve the outstanding problem of the method by which the proposed JET council will work, the way will be clear for an early Council of Ministers meeting to finalise the question of the site, which is expected to be either Garching in Germany or Culham in England.

Argentinian disappears

The latest Argentinian scientist about whom concern is being expressed is Horacio Dottori, an astrophysicist. Sr Dottori was at the Cordoba Astronomical Observatory from 1967 to 1976 except for a two-year period in Germany at the Max Planck Institut für Physik und Astrophysik from 1971–73.

He worked on observations of peculiar and interacting galaxies. In March 1976, following the military takeover, he was dismissed. He was arrested in August 1976 and has now disappeared; his friends believe he has been sent to a camp called 'La Perla', about which little is known.

X-ray survey

To meet the requirements of a directive on radiological protection from the EEC Council of Ministers, and because existing information in Britain is out of date, the UK National Radiological Protection Board (NRPB) is to conduct a survey, beginning in June and encompassing over 100 National Health Service hospitals, of the radiation doses which patients receive from the diagnostic use of X-rays.

The medical use of radiation contributes some 13% of the total dose which the population receives, making it the largest man-made component. Natural background radiation con-

tributes some 84%. The specific objective of the survey is an estimation of the so-called 'genetically significant dose' (GSD) to the population arising from diagnostic radiology.

Chemistry PhD survey

The Chemical Society's Standing Advisory Committee on Relationships between Higher Education and Industry (SACRHEI) recently completed a survey on US views of the British chemistry PhD. It sought the opinions of 40 US industrialists, seven US professors of chemistry and a couple of professional associations. Although about half the industrialists and academics thought the British and American PhDs comparable so far as research is concerned, the industrialists thought holders of British chemistry PhDs were less motivated towards employment in industry and had less appreciation of overall industrial problems than their American counterparts.

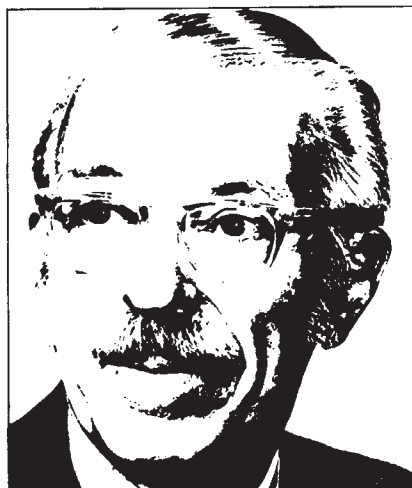
THE ban on saccharin proposed by the Food and Drug Administration (FDA) has unleashed a public reaction of unexpected, and allegedly unprecedented, intensity. The protest against the ban was apparently expected to last for only a few days and, accordingly, the US manufacturer of saccharin announced plans to discontinue production. After a week, these plans were cancelled because of the heavy and continuing demand for saccharin by consumers who were stockpiling it in various forms. This must have been a great surprise to those who thought that mere mention of carcinogenesis would make the public abjure saccharin.

I have received copies of about 150 US newspaper articles on the ban. The FDA came in for a tremendous clobbering, even though its action was mandatory under provisions of the Delaney Clause of the Federal Food Drug and Cosmetic Act. In former days, those who objected to the Clause were often rebutted by *ad hominem* accusations, as for example by Epstein (*Preventive Medicine* 2, 140, 1973):

All such criticisms [of the Delaney Clause] have emerged from industrial groups, trade associations and their consultants, and from groups that are clearly identified with protection of industrial interest . . . Such 'captive' spokesmen [are characterised by] lack of expertise and national recognition in the field of chemical carcinogenesis . . . No such criticisms have emerged . . . from qualified scientific representatives of citizen, consumer and public interest groups.

In the face of such invective, a

symposium on the Delaney Clause, held by the New York Academy of Sciences in 1973, did not produce a single proposal for its revision. Banning saccharin seems to have changed the picture. As a columnist said, "It wasn't large corporation people who

Consumer revolt

THOMAS H. JUKES

swept through supermarkets, cleaning the shelves of artificially sweetened products".

The FDA, perhaps intentionally, noted that "a human would have to drink 800 12-ounce cans of diet soda a day for a lifetime" to ingest an amount of saccharin comparable to that received by rats in the Canadian study that led to the ban. In vain did

FDA point out that one can daily would still impose a proportionately lesser risk. Cartoonists, columnists, and lawmakers swooped down gleefully on the 800-can statistic. One cartoon showed a pharmacist offering a frustrated saccharin customer cigarettes and whisky as an alternative for the banned sweetener. A congressman sought fleeting fame by introducing a bill to prohibit giving saccharin to rats. "Science For The People" had taken over, but not in the way that its sponsors had originally planned. A few stern hard-liners told diabetics to stop griping, and drink water, a sort of Marie-Antoinette-in-reverse suggestion that was not well received.

Public rebuttal of the Delaney Clause received support from eminent clinicians who said they had seen practically no cases of bladder cancer in diabetics who had been on saccharin for many years, thus implying that rats responded differently from human beings. Thus the two cardinal points of the Delaney Clause: extrapolation of carcinogenesis from laboratory animals to human beings, and the absence of a threshold, both were widely discounted. The Delaney Clause may well need revisions. However, let us hope that opposition to banning saccharin will not jeopardise a programme to reduce exposure to environmental carcinogens.

As of last reports, the FDA was still answering telephone calls, but Congressman James Delaney could not be reached.

correspondence

Rights of scientists

SIR,—You quote the newly published report *Scholarly Freedom and Human Rights* (24 February, page 671) in stressing the responsibility of learned societies to support oppressed and persecuted scientists by public protests. This is important: hitherto it has usually been argued that only non-scientific channels are permissible for such protests because actions taken by scientific societies would be political demonstrations not consistent with their high scientific aims.

Two points seem to be disregarded in this argument. Firstly, that protests through non-scientific channels emphasise the humanitarian aspect whereas the professional aspect is emphasised only through scientific societies. If a scientist is hindered or restricted in his work and prevented from normal communication and exchange with his colleagues within the international scientific community, not only is his own work impeded but also that of his colleagues and hence scientific progress in general. Secondly, that the governments that persecute scientists bring politics into science whereas the scientific societies submit their professional protests just to keep politics out of science.

It has also been argued that international societies should be particularly careful in such matters, whereas national societies might act more freely. However, there are good reasons for the view that an international scientific society is an appropriate channel for appeals and protests when scientists are arbitrarily cut off from the international forum of scientific discussion. The very purpose of an international scientific society is to promote science by fostering international collaboration, communication and exchange among scientists. A national society is involved in professional, educational and advisory activities, and the promotion of international cooperation, which is the main concern of an international society, is of but minor importance. If a member of an international society is prevented from normal communication and exchange with fellow-scientists in other countries, the very purpose of the society is violated and it is the duty of its board to take measures to restore the member to a normal scientific life. Although practical considerations may call for restraint and moderation while acting within an international body, it is

important that the principle is made clear. It is the scientific and professional aspect of the matter that should be advanced in this context; political and other arguments should be avoided.

In conclusion, then, it is the duty of scientific societies to speak up officially in defence of oppressed and persecuted scientists.

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The Tacoma Bridge collapse

SIR,—Dr Henry Chilver (10 February, page 494) reviewed a number of accidents and attempted to categorise them by making use of a 'triangle of failures'. The failure of the Tacoma Bridge in 1940 lies in Chilver's diagram midway between 'unknown environmental forces' and 'unpredictable behaviour' and he says that "The cause of the accident was an inadequate understanding of the interaction of the structure with its environment, leading to large oscillations of the bridge. The resulting behaviour was unpredictable at the time . . .". There were however indications in information available at that time, but not collated then, that a failure would occur and that the mode of failure was not new. The figure shows variation of span length, L , of a suspension bridge, with the year of building. Also shown are corresponding values of the ratio of girder depth, d , to span length (some examples are missing because records are incomplete); this parameter is a rough measure of the stiffness of the girder against vertical loads from wind or traffic. In the 19th century, bridges were designed on an intuitive basis and several were destroyed or damaged by winds. In one or two instances, eye witness reports were recorded and these bear remarkable similarity to the observations recorded on film during the collapse at Tacoma. The earlier collapses consistently occurred whenever d/L was less than approximately 0.006.

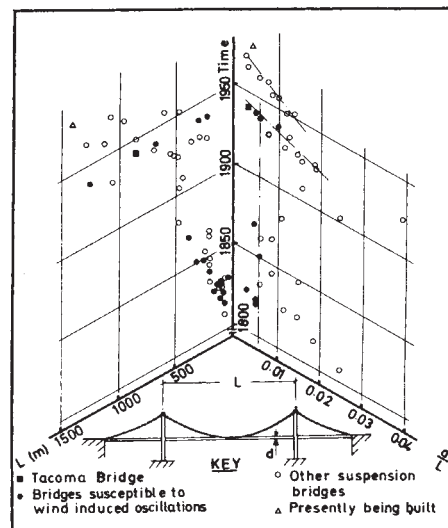
At the turn of the century a new theory was developed which seemingly gave mathematical rigour to the design of the deck girder. This theory considered only static wind pressure loading but, for the heavy, deep girders then currently fashionable, it proved very successful and no dynamic behaviour was observed. During the

next thirty years several suspension bridges were built and, with the confidence instilled in the designers by the availability of the theory, there was a trend to much lighter girders (d/L). Economy, lower traffic loads and aesthetic appeal were the main driving forces in this move. Eventually, as the figure shows, the values of d/L dropped below 0.006 and wind induced oscillations were observed in a number of bridges, although only the Tacoma Bridge actually collapsed. After that deck girders were made stiffer, but the pattern of development was quickly re-established. (This time, however, the critical value of d/L has been safely reduced because of the use of wind-tunnel testing in conjunction with the design calculations).

Had proper records been kept of trends in bridge design, and had engineers been made aware of earlier wind-induced failures, a warning would have been sounded on the dangers of using the analysis for very light deck girders. We have shown that the failures of other bridges of different types could also have been avoided if records had been kept of design trends and minor accidents preceding the major event had been adequately investigated. Similar trends have been noted in structures other than bridges. We suggest the need for a facility to gather and process information on which to base the direction of research on structural behaviour.

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news and views

Another optical pulsar

from Jocelyn Bell Burnell

EVER since the discovery of optical flashes from the pulsar in the Crab Nebula and the association of pulsation in this band with rapid pulsation period, astronomers have expected that the Vela pulsar, the third fastest, should likewise emit pulses of light. But in the 8 years since that initial discovery hope has gradually faded as larger and larger telescopes have searched for fainter and fainter flashes. So far had faith dimmed that consideration was recently given to the unpulsed optical emission of the pulsar, and an attempt made to pick out the candidate star on the basis of predicted magnitude and colour (Lasker *Astrophys. J.* **203**, 193; 1976).

But at last, optical pulsations have been found. In this issue of *Nature* (page 692) Wallace and eleven others (in a paper with more authors than paragraphs) report the detection of optical pulsations from the Vela pulsar. In a collaborative effort between optical astronomers from the Royal Greenwich Observatory and the Anglo-Australian Telescope, and radio astronomers in Australia, faint optical pulses at the same pulsation period as the radio pulses have been recorded. With a time-averaged magnitude of 25.2 this is the faintest thing ever seen (and in good agreement with Pacini's prediction that it would have magnitude about 25 (*Astrophys. J.* **163**, L17; 1971)).

The Vela pulsar has been a particularly troublesome pulsar to deal with. Not only are the light pulsations weak, requiring a large modern telescope such as the AAT with sophisticated equipment for analysis, but the pulsation period of the pulsar itself, as observed by the radio astronomers, is not stable. Pulsars are believed to be rotating neutron stars—stars of a few kilometres radius with a density comparable to that found in the atomic nucleus. The pulsation period is the

rotation period, which in the case of the Vela pulsar is 80 ms. The period gradually lengthens as the star loses rotational energy, and, again for the Vela pulsar, this is about 11 ns per day. This is typical pulsar behaviour, although for both the Crab and Vela pulsars the rotation rates are much faster than average and the slowing more noticeable. What is peculiar to the Vela pulsar and partly responsible for the delay in the discovery of the light flashes is the occasional large hic-cough or "glitch" of the pulsar, when its rotation rate suddenly increases (typically by 200 ns). The position of a radio pulsar is obtained by the radio astronomers from a study of the Doppler shifts in its pulsation period due to the annual motion of the Earth about the Sun. Erratic behaviour of the pulsar period upsets the determination and uncertainties in the position of this pulsar have not helped the optical astronomers.

The region around the Vela pulsar, PSR 0833-45, is complex. There are many faint stars, and the remains of a supernova—a star that exploded cataclysmically blowing off a shell of material. The pulsar, which may have been formed by the supernova explosion, lies within part of this shell—the part called Vela X by radio astronomers. To add confusion to complexity there are two X-ray sources in the constellation of Vela, Vela X-1 (3U0900-40) and Vela XR-1 (3U0833-45). Vela X-1 shows strong X-ray pulsations whereas Vela XR-1 which is presumably associated with the pulsar does not!

According to Pacini's predictions the pulsed X-ray emission from 0833-45 should be below the threshold of present X-ray telescopes, but γ -ray astronomers have had noticeable success in detecting this pulsar. (The division between X and γ -ray astronomy is made on the basis of photon energy,

the divide being around a few hundred keV, and is independent of the method of production of the photons.) So successful have been the γ -ray astronomers (with the COS B satellite, for example), that one wonders whether it might not be reasonably strong in X rays too. It will be interesting to learn more about the X-ray source: where it is in relation to the pulsar, what it is, and what fraction of the X-ray emission is pulsed.

It is tempting to assume that the Vela pulsar is similar to the Crab only less energetic: both are rapid pulsars, both emit pulses at the radio pulse period over a wide range of the electromagnetic spectrum and at γ -ray energies their pulse profiles are strikingly similar. But there are striking differences too, notably that whereas for the Crab the radio, optical, X- and γ -ray pulses are all in phase, in the Vela pulsar the radio pulse apparently precedes the optical and γ -ray pulse.

One is reluctant to divide a sample of two into two separate categories, and, unfortunately, there are unlikely to be many more samples on which to establish such a division. This makes this discovery and the consequent observations all the more important. □

Correction

Changes in proof to the article by Roberts and Falkow in last week's *Nature* (**266**, 630; 1977) require the following correction to be made to the accompanying comment in *News and Views* (**266**, 586; 1977). In paragraph 3 it is stated that the 25 Mdal sex-factor plasmid has not yet been found to be transferred to recipient strains along with the drug resistance plasmid. Roberts and Falkow have now found that it is transferred to recipient strains of *Neisseria gonorrhoeae*.

Synaptic memory in the hippocampus

from Shin-Ho Chung

It has been known for some time that efficiency in synaptic transmission can be enhanced for several hours after pre-synaptic fibres have been briefly stimulated. Interest in this phenomenon, known as 'long-lasting potentiation', is partly due to the belief that such a change in synaptic efficiency may well be a neurophysiological mechanism for storage of information in the central nervous system. While most physiological studies on synapses have emphasised events occurring immediately after the arrival of a nerve impulse, psychological observations reveal many phenomena which must be due to long-lasting effects of nerve impulses on synaptic pathways. Amongst these are the after-effects of intense sensory stimulation, which may persist for many days, as well as conditioned reflexes, and the process of learning; all these are almost certainly due to long-lasting changes in the properties of neurones and synapses brought about by use and disuse. A number of recent studies are aimed at elucidating the underlying mechanisms of synaptic plasticity.

Long-lasting potentiation in a mammalian synaptic pathway was first discovered by Larrabee and Bronk (*J. Neurophysiol.* **10**, 139; 1947) and was later confirmed by Lloyd (*J. gen. Physiol.* **33**, 147; 1949). In a simple synaptic pathway where the presynaptic axons connect directly to the post-synaptic neurones, they noted that transmission through the pathway is greatly enhanced for several minutes following a brief period of repetitive stimulation of the presynaptic axons. The duration of this facilitation could be extended for up to 2 hours by stimulating the pathway at an optimal frequency (Beswick & Conroy *J. Physiol. Lond.* **180**, 134; 1965). Bliss & Lomo (*J. Physiol. Lond.* **232**, 331; 1973) later extended this observation to the hippocampus, which proved to be a particularly suitable structure for electrophysiological analysis of synaptic plasticity. Cells there form tightly packed layers, with their dendrites oriented radially, and afferent inputs originating from different regions of the brain terminate at discrete segments of the dendrites (see diagram on page 738 of this issue of *Nature*). Brief episodes of repetitive stimulation to the perforant path fibres, which link the entorhinal cortex with the granule cells of the hippocampus, produce a cumulative increase in the amplitude of the responses evoked by subsequent single stimuli. Compared with the spinal cord (Lloyd *op. cit.*; Beswick & Conroy *op.*

cit.), the duration of synaptic potentiation in the hippocampus is prolonged, and the degree of facilitation pronounced. For example, a few brief trains of repetitive stimulation increase the amplitude of the synaptic potential by as much as 300% and this enhanced synaptic efficiency persists, in certain conditions, as long as several weeks (Bliss & Gardner-Medwin *J. Physiol. Lond.* **232**, 357; 1973). Since these initial reports, the phenomenon has been confirmed in various mammalian species and in two other hippocampal pathways (Deadwyler *et al.* *Brain Res.* **88**, 80; 1975; Douglas & Goddard *Brain Res.* **86**, 205; 1975; Schwartzkroin & Wester *Brain Res.* **89**, 107; 1975; Dudek *et al.* *J. Neurophysiol.* **39**, 384; 1976).

An unresolved question, which Anderson *et al.* (page 736 of this issue of *Nature*) and Lynch *et al.* (page 737) have sought to answer, is whether the enhanced synaptic efficiency seen in the conditioned pathway is due to a generalised increase of sensitivity in the postsynaptic neurones, or whether it is confined to those synapses which have been repetitively activated (or tetanised). Although the findings reported by the two groups differ in detail, it is now satisfactorily established that a prolonged increase in synaptic efficiency is confined to the tetanised pathway, suggesting that the underlying processes giving rise to the hippocampal potentiation may differ from those responsible for the heterosynaptic facilitation which occurs in certain invertebrate neurones (Kandel & Tauc *Nature* **202**, 145; 1964; *J. Physiol. Lond.* **181**, 1; 1965). Andersen and his colleagues report that a tetanus applied to one group of afferents causes no change in synaptic transmission in the untetanised pathway, while Lynch and his coworkers claim that the enhanced synaptic efficiency in the tetanised pathway is accompanied by a generalised depression of the postsynaptic neurones. This latter result is consistent with their previous finding that the sensitivity of pyramidal cells to iontophoretically applied glutamic acid is decreased after tetanus (Lynch *et al.* *Nature* **263**, 151; 1976). While the conflicting observations reported by the two groups are difficult to reconcile, they are only tangential to the ultimate aim of the investigation, which is to localise the changes in the properties of neurones and synapses caused by use and disuse, and to understand the ways in which these changes are induced.

There are a number of possible mechanisms which may be responsible for long-lasting potentiation (see Bliss & Lomo *op. cit.*). For example, an impulse flowing down the previously tetanised pathway may invade more terminals than normal, thereby producing a larger effect on its target cells (see *News and Views, Nature*, **264**, 313; 1976). Alternatively, and this is the possibility which Andersen *et al.* favour, the same number of terminals may be activated but each terminal may liberate an increased amount of transmitter. Finally, it is also possible that previous activity may increase the sensitivity of the postsynaptic junctional membrane; for example, Rall (*Biophys. J.* **2**, 145; 1962), among others, has postulated that a structural alteration of the postsynaptic spines may be an important variable in changing the relative weights of synaptic inputs. The swelling of the spines, due to the uptake of electrolytes and water, can cause a reduction in the resistance of the narrow stems by which the spines are attached to the parent dendrites, and this could provide a basic mechanism for long-lasting potentiation in this monosynaptic pathway. In this context, it is relevant to note that the diameter of spines in the hippocampus appears to increase abruptly when the pathway innervating them is tetanised (van Harreveld & Firkova *Anat. Rec.* **181**, 355; 1975; *Expl Neurol.* **49**, 736; 1975).

The molecular basis for long-lasting potentiation will remain speculative until synaptic transmitters in the central nervous system are identified, and this is proving an elusive task. An excellent study in the amphibian sympathetic ganglion, where the synapses are known to be mediated by acetylcholine, has demonstrated that a slow decrease in membrane conductance, triggered by muscarinic receptors, causes potentiation of synaptic responses generated by the activation of nicotinic receptors (Schulman & Weight *Science* **194**, 1437; 1976). Although the mechanism of potentiation in the hippocampal pathways may not be the same as in the amphibian sympathetic ganglion, it is this type of controlled study which is now needed for cortical cells. Once the underlying mechanism governing plasticity observed in the simplest synaptic system is elucidated, experimental investigation can then be extended to the more complex polysynaptic pathways and, finally, to the grey matter of the cerebral cortex. This

ultimate aim, however, will not be achieved in the near future. As Ramón y Cajal once remarked, the structure of the cerebral grey matter is so in-

tricate that it defies and will continue to defy for many decades the obstinate curiosity of neurobiologists.

□

Anti-anxiety receptors in the brain?

from Leslie Iversen

LIGAND binding techniques are well established as important tools for studies of a variety of biological receptors for peptide hormones and neurotransmitter substances. In most cases such assays have been developed to investigate receptors for which the naturally occurring ligand is already known, for example, insulin, acetylcholine or noradrenaline. In the case of the opiate receptor, however, the discovery of the high affinity binding of radioactively labelled morphine-like drugs to membranes in brain homogenates (Pert & Snyder *Science*, **179**, 1011; 1973) was of a different character, since it allowed description of the precise characteristics and distribution of a receptor mechanism for which no naturally occurring ligand was then known, and it offered a powerful tool for the subsequent discovery of the enkephalins and endorphins as a new class of naturally occurring agonists for a receptor mechanism hitherto described only in terms of the organism's response to opiate drugs.

Such drugs, however, represent only one of several important classes of centrally acting drugs whose pharmacological mechanisms remain obscure. Squires and Braestrup (page 732 of this issue of *Nature*) now describe their preliminary results in applying a similar rationale to studies of the receptor mechanisms possibly involved in mediating the actions of minor tranquillisers of the benzodiazepine class. These drugs, exemplified by the anti-anxiety agent diazepam (Valium) and the hypnotic drug nitrazepam (Mogadon), have had an enormous commercial success since the discovery of their remarkable psychopharmacological properties in the 1950s. They, and many related analogues in the benzodiazepine series, are able to tame otherwise aggressive laboratory animals, they exhibit CNS muscle relaxant properties, and in man the drugs are used as anticonvulsants and more importantly as anti-anxiety agents. At higher doses they are also effective hypnotics, and since they are much less toxic than barbiturates, have taken an increasing share of the large market for those suffering from anxiety and/or insomnia. Benzodiazepines,

needless to say, have been consumed by many millions of people in the industrialised nations of the world in which such complaints are endemic.

Despite their unique pharmacological properties and widespread medical use, the mode of action of the benzodiazepines remains unknown. There have been various attempts to explain their effects in terms of current neuropharmacological fashion, that is, by action on CNS catecholamine or indolamine transmitters, but these have been largely unconvincing. Young *et al.* (*Proc. natn. Acad. Sci. U.S.A.* **71**, 2246; 1974) found that the potencies of a series of benzodiazepines in displacing radioactively labelled strychnine from binding sites associated with glycine receptors in mammalian spinal cord correlated fairly well with the potencies of the same drugs in various animal behaviour tests predictive of anti-anxiety properties, and these authors proposed the hypothesis that the drugs might interact with receptors for this inhibitory amino acid transmitter in CNS. However, relatively high concentrations of the drugs were needed to show this effect and subsequent neurophysiological experiments failed to lend support to this hypothesis (Curtis *et al. Brit. J. Pharmac.* **56**, 307; 1976). A more recent proposal has been that the benzodiazepines might in some way mimic or enhance the effects of another inhibitory amino acid transmitter, γ -aminobutyric acid (GABA) at CNS receptor sites. This hypothesis was based on both biochemical and neurophysiological evidence (Polc *et al. N. S. Archiv. Pharmac.* **284**, 319; 1974; Costa *et al. Adv. Biochem. Psychopharmac.* **14**, 113; 1975), and has attracted a wide following. Nevertheless, it has proved difficult to demonstrate any direct interaction between benzodiazepines and GABA receptors, although recent neurophysiological evidence has shown that these drugs are able to exert inhibitory effects on the firing of single cells in rat brain similar to those seen on application of GABA (Dray & Straughan *J. Pharm. Pharmac.* **28**, 314; 1976).

Squires and Braestrup found that high specific activity ^3H -diazepam is bound to saturable sites in rat brain

membrane preparations with very high affinity—half saturation being achieved at a drug concentration of only 2.6 nM. When low concentrations of the labelled drug were used more than 90% of the total binding was attributable to this single class of high affinity sites. More importantly, they showed that the potencies of 21 different non-radioactive benzodiazepine drugs in competing with labelled diazepam for binding showed a highly significant correlation with the known pharmacological potencies of these drugs determined previously in various animal tests known to be predictive for anti-anxiety properties in man. The potencies of the drugs tested in both the *in vivo* and *in vitro* tests ranged over four orders of magnitude. On the other hand, none of the known amine or amino acid transmitters (including glycine and GABA), or any of the drugs known to interact with their receptors, had any inhibitory effects on ^3H -diazepam binding. Other minor tranquillisers, such as meprobamate, barbiturates or ethanol, were also ineffective as inhibitors, as were opiate drugs.

The authors therefore, claim to have described a saturable high affinity binding mechanism whose pharmacological specificity suggests that it may have some important relation to the mode of action of the benzodiazepines in whole animal experiments or in man. It is also interesting to note that the highest density of ^3H -diazepam binding sites was found in the frontal and occipital cortex of rat brain, areas not known to be enriched in any of the known transmitter substances.

If their hypothesis is correct, and caution is certainly still needed in extrapolating from these preliminary biochemical results, their findings may have a major impact on our future understanding of the mode of action of this class of psychotropic drugs. By analogy with the discovery of the opiate receptor, the benzodiazepine receptor assay may even offer a simple means for the discovery of the naturally occurring ligand for such receptors—the brain's own anti-anxiety substance?

Further developments in this field will certainly be awaited—anxiously.

A hundred years ago

At the last meeting of the French Anthropological Society, a long report was read which showed that Druidism was not quite extinct in Brittany, some country people still adhering to Pagan practices in spite of the priests' exertions. It was noticed that the clergy were anxious to destroy menhirs and other similar relics. A petition has been sent to the ministry to put a stop to this iconoclastic zeal.

From *Nature*, **15** 19 April, 539; 1877.

SIN and the muon-electron puzzle

from F. E. Close

DURING the past few weeks several papers have appeared proposing mechanisms to explain the exotic radiative transmutation of the muon into the electron. Although widespread publicity in the world press may have led readers to think that this 'forbidden' decay has been seen (hence the sudden flux of theoretical papers) no one involved in the experiment at the Swiss Institute for Nuclear Research (SIN) in Zurich has yet claimed to have solid evidence for it. Indeed, the group concerned are still quoting a limit consistent with no such decays at a level of about one part in a hundred million of all muon decays. The rumours, and source of the press reports, were that a signal was being seen at the level of order one part in 10^8 . However, there are experimental questions still to be settled, for example, the energy and angular resolutions which limit conclusions at present: hence the present claim only of a limit.

Why all the fuss? The reason is that for over a quarter of a century the muon has remained a mystery. So far as we know the Universe could have existed without a muon at all, and our everyday experiences in such a Universe would have been the same as in the real world (apart from esoteric phenomena like the pion lifetime). Yet for some reason nature is not satisfied with the electron and its associated neutrino and has repeated itself by invoking two more leptons (the muon and its neutrino).

The muon is identical to the electron in all respects except that it is about 200 times as massive. The question 'why does the muon weigh?' has remained unanswered for 30 years. No evidence for a new interaction possessed by the muon has been found, which would

explain its larger mass and distinguish it from the electron. In all respects the muon appears to be simply a heavy electron and yet does not decay radiatively into one. It seems that the muon remembers that it is a muon partnered with its own neutrino and so

$$\mu^- \rightarrow \nu_\mu + (e^- + \bar{\nu}_e)$$

occurs but decay modes like $\mu^- \rightarrow e^- \gamma$, $e^- e^-$ and so on are not seen. A rule was therefore invented to dignify these observations: muon number (possessed only by the muon and its neutrino) is conserved in nature. Beyond this little or no progress was made.

Early searches for the radiative decay $\mu \rightarrow e \gamma$ were made and Pontecorvo and Hincks found a limit of a few per cent of all decays. Over the years this limit has been greatly improved and today stands at the level of one part in a hundred million. In principle experiments currently in progress at SIN in Zurich and at TRIUMF in Canada will either see a signal or place new limits of order one part in a thousand million. There are reports of an experiment planned at Los Alamos, New Mexico, which may be able to go down to a sensitivity of 1 part in 10^{10} .

The dramatic significance of these limits may be appreciated when one realises that only the known muon decay mode $\mu \rightarrow e \bar{\nu}$ is a typical weak interaction. Hence one is failing to see $\mu \rightarrow e \gamma$ (naively an electromagnetic transition) at less than one hundred millionth of a weak decay rate (this latter being the weakest interaction apart from gravity that is known to exist). Hence, if there are any undreamt of subtle effects in the weak interactions then it may well turn out that they will show up first in the $\mu \rightarrow e \gamma$ amplitude.

Gauge theories and massive neutrinos

The discoveries of charmed particles and their intimate relation with the gauge theories have painted a clear and beautiful picture of nature. An intimate deep relation has been noticed between the lepton world and the quark world, more specifically the $(\mu \nu_\mu)$ pair *vis à vis* the $(e \nu_e)$ pair in the leptons on the one hand and the charmed-strange quark pair *vis à vis* the up-down quarks in the hadron world on the other. In the future this may point towards a unification of leptons and quarks (or weak-electromagnetic and strong interactions!). At present it has made theorists think again about the role of the muon in nature's scheme—why it exists and why it does not decay radiatively into the electron. To appreciate these ideas it is useful first to describe the salient points

of the current theory and then describe the new ideas on the application to the muon and its decays.

The carriers of the electromagnetic and weak interactions are the photon and the W boson respectively. When these fields interact with leptons or with quarks they can cause transmutations only within the left-handed doublets of

leptons: $\begin{bmatrix} \nu_e \\ e \end{bmatrix}$ and quarks: $\begin{bmatrix} u \\ d \end{bmatrix}$ and $\begin{bmatrix} c \\ s \end{bmatrix}$

Quarks d, s with well defined mass (eigenstates of the strong interactions) are linear combinations of the d' and s'

$$\begin{aligned} d' &= d \cos \theta + s \sin \theta \\ s' &= -d \sin \theta + s \cos \theta. \end{aligned}$$

It is as if the strong interaction world is rotated by a small angle θ (the Cabibbo angle) relative to that of the weak interactions. Hence the weak interactions can, and do, cause transitions between the (ud) quark doublet and the (cs) doublet. It is by this 'leakage' that the Λ beta decay, $\Lambda \rightarrow p e \bar{\nu}_e$ occurs and by which the charmed particles decay

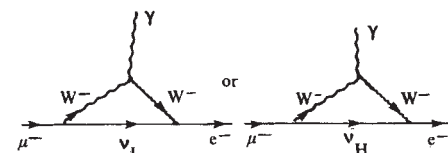
$$\begin{cases} c \rightarrow s' \equiv s \cos \theta - d \sin \theta \\ D^0(c\bar{u}) \rightarrow K^-(s\bar{u})\pi^+ \end{cases}$$

This mechanism for charmed decay is known as the GIM mechanism (see *Nature* 262, 537; 1976) due to S. Glashow, J. Iliopoulos and L. Maiani. Is there an analogous mixing and GIM mechanism for the lepton doublets? In principle the answer is yes, and a consequence is that a leakage from muon world to electron world can arise leading in particular to the radiative decay $\mu \rightarrow e \gamma$. How does this come about?

Suppose that the two neutrinos have different masses. Then we can define ν_L and ν_H for the lighter and heavier respectively and these will play the part of the d and s quarks. The partners of the electron and muon in weak interactions will be defined as ν_e and ν_μ (these playing the part of the d' and s' quarks). Then analogous to the quark system the $\nu_{L,H}$ may be orthogonal mixtures of ν_e, ν_μ .

$$\begin{aligned} \nu_e &= \nu_L \cos \phi + \nu_H \sin \phi \\ \nu_\mu &= -\nu_L \sin \phi + \nu_H \cos \phi \end{aligned}$$

the decay $\mu \rightarrow e \gamma$ can then proceed for instance by the processes



If the L and H neutrinos have the same mass (in particular being both massless) then there is exact cancellation

Key

γ , photon

Leptons

e , electron
 e^+ , positron
 ν_e , electron neutrino
 $\bar{\nu}_e$, electron antineutrino
 μ , muon
 ν_μ , muon neutrino
 $\bar{\nu}_\mu$, muon antineutrino

Hadrons

p, proton
 Λ , lambda
 π , pion
K, kaon
 D^0 , neutral charmed meson

between the two and the decay mode vanishes. However, if there is a mass difference then the amplitude is finally proportional to $m_H - m_L$ scaled by m_W , the mass of the W boson.

The W boson is believed to have a mass of around 60 GeV. The mass difference of the two neutrinos is at most some 650 keV (it could even be zero) and so the predicted rate can at most be

$$(\mu \rightarrow e\gamma)/(\mu \rightarrow \text{all}) \lesssim 10^{-25}$$

which is far below the present limits.

New heavy leptons

In the light of the above, what price must we pay if the decay were found at a level of 1 in 10^9 or so? This could have been accommodated in the above arguments if the heavy neutrino has a mass of several GeV, far in excess of the known limit. Could there be further heavy leptons in nature which could help in this respect? There is now good evidence for a heavy charged lepton τ around 2 GeV in mass, probably accompanied by a neutral ν_τ . The latter has a mass less than 700 MeV (Perl *Phys. Lett.* **63B**, 466) and so cannot be of use in the present context. However, this discovery does release one's inhibitions and shows that a whole new spectroscopy of heavy leptons is not necessarily absurd.

If such further heavy leptons indeed exist then the $\mu \rightarrow e\gamma$ decay can arise and several mechanisms have been suggested. One way is to have right handed doublets involving new neutrals and the electron or muon. With the massive neutrals introduced this way the previous game can be played and a sizeable $\mu \rightarrow e\gamma$ decay accommodated. This idea has been proposed by T. Cheng and L. Li in the USA. An interesting by-product could arise in connection with the failure to see parity violation in atoms. Parity violation occurs if the electron (muon) only takes part in left handed weak interactions. If the electron (muon) now also couple to heavy neutral leptons in the right handed mode, parity can be conserved. (Of course, parity will still be violated in neutron β decay as the neutron-proton mass difference is so small that only the electron and its massless left-handed neutrino can be produced). In a similar vein, F. Wilczek and A. Zee of Princeton University have proposed doubly charged heavy leptons to generate the μ decay.

Before we conclude that the observation of $\mu \rightarrow e\gamma$ would force us to deduce that heavy leptons exist we should notice a proposal of J. Bjorken and S. Weinberg of Stanford, California. In the gauge theories, particles gain masses by coupling to scalar fields known as Higgs particles. The coupling of the Higgs particles to fermions can generate contributions to weak interaction decay rates. However

this is usually ignored since the coupling is proportional in strength to the masses of the fermions concerned, and the electron and muon are very light. In rare and ultrarare decay processes these couplings could turn out to have important phenomenological consequences. Furthermore, Bjorken and Weinberg noted that in the standard Weinberg-Salam gauge theory one can have a naturally occurring coupling of a Higgs particle, a muon and an electron all at one point and hence generating the transition $\mu \rightarrow e\gamma$ without extending the number of leptons in nature beyond the famous four.

Before the advent of gauge theories an observation of $\mu \rightarrow e\gamma$ would have left us puzzling as to how to proceed. With the great advances of the past few years not only do we know how to tackle the problem but even have several solutions in advance of any signal! Perhaps none of the models is very suavis. However, if a signal is seen in the current experiments then one must take these ideas seriously and more impressive support for the gauge theories will have been unearthed. That this will happen in the next month or two is many theorists' midsummer night's dream—but it could turn out to be much ado about nothing.

Spin waves in superfluid ^3He

from P. V. E. McClintock

ONE of the most intriguing features of the recently discovered superfluid phases of liquid ^3He is that in sharp contrast to ^4He , the only other superfluid known in nature, they have magnetic properties. It is hardly surprising, therefore, that efforts to understand superfluid ^3He have been influenced by making comparisons with more conventional types of magnetic material, attempting to explore both the similarities and the fundamental differences in their properties. One characteristic feature of ordered magnetic solids is that they may support so-called spin waves, a form of collective excitation among the magnetic elements. The possible existence of spin waves in ^3He has consequently been a subject of much discussion during the four years which have elapsed since the superfluid phases were discovered by D. D. Osheroff, then working at Cornell University. It is of particular interest, therefore, that Osheroff and his co-workers at Bell Laboratories have now reported (*Phys. Rev. Lett.* **38**, 134; 1977) the first experimental observation of spin waves in the B phase of superfluid ^3He .

The magnetism of liquid ^3He arises from the magnetic moments carried by the nuclei of the ^3He atoms. In ordinary normal liquid ^3He in the absence of a magnetic field the nuclei are so weakly coupled to each other that the liquid is completely devoid of any overall magnetic order. When the liquid is sufficiently cooled, however, things become very different: the onset of long range order at the superfluid transition temperature involves the orientation of nuclear spins in definite directions, producing just the sort of ordered magnetic structure which might be expected to support spin waves.

In the case of a magnetic metal, one of the most convenient ways of demonstrating the existence of spin waves is through use of a resonance technique to excite standing waves in a very thin layer of the material. The situation is somewhat analogous to the more familiar one of standing waves on a stretched string whose ends are fixed in position. Unlike the case of the string, however, it is not the position, but rather the direction of the spins which is fixed on the boundaries of the material and which varies coherently through its thickness. Absorption of energy takes place for radio waves of the right frequency to excite a standing spin wave, that is, one such that the thickness of the layer of metal is equal to an integral number of half-wavelengths. Thus, if the rate of absorption of electromagnetic radiation is measured while its frequency is gradually increased, a series of peaks will be seen corresponding respectively to the fundamental, and higher orders of standing spin waves being excited.

The Bell Laboratories group used what in many ways is a very similar technique in their search for spin waves in superfluid ^3He . The combination of a strong magnetic field and the presence of a solid surface was used to fix the spin anisotropy axis n , thus defining the directions of the spins at the surfaces of a series of thin laminae of liquid. These were formed between a set of 20 fused quartz plates each about 7×11 mm in area, spaced $210 \mu\text{m}$ apart. The magnetic field was applied in the plane of the plates. Under these conditions, although n tries to lie parallel to the magnetic field in the bulk liquid between the plates, it is compelled to take up a different fixed direction where the liquid touches the surfaces of the plates. The competition between these effects causes the direction of n to vary smoothly with position in a completely determined way between the plates. Spin waves consist, therefore, of coherent deviations from this equilibrium situation, and may be expected to reveal their existence, as in the case

of the thin metallic film, through the resonant absorption of electromagnetic radiation at particular frequencies depending, in this case, on the temperature and on the magnitude of the applied magnetic field. The cell was placed in a compressional cooling apparatus in which the temperature of the liquid was lowered by reducing its volume and thus solidifying some of it, which was able to reach the so-called superfluid B phase which is stable below its transition temperature at about 2 mK.

In the event, a series of striking absorption peaks was indeed found approximately at the frequencies predicted by theory. Although the peaks were broader than ordinary NMR resonances in ^3He , they were quite well defined, thus eliminating the lurking possibility that spin waves in ^3He might be modes which are overdamped and therefore unobservable. As the authors point out, it is quite possible that the observed width of the resonance maxima is merely an experimental effect arising from small variations in the spacing of the quartz plates. The change with temperature of the resonant frequencies turned out qualitatively to be very much in line with theoretical expectations.

The experimental results are not, however, in close quantitative agreement with theory. However, although the authors' tentative explanation of the discrepancies (typically about 20%) may or may not be correct, there seems little doubt that they were indeed observing spin waves. Further experimental and theoretical work is clearly required, but it seems that spin wave resonance has now been added to the rapidly growing battery of techniques available for elucidating the dauntingly complicated properties of superfluid ^3He . □

Complementary genetics

from M. J. Hobart

An EMBO Workshop on Complementary Genetics was held in Cambridge, UK on 18–22 March, 1977. It was organised by Dr P. Lachmann, MRC Group on Mechanisms in Tumour Immunity, Cambridge.

THE genetics of the complement system were put on the map, both chromosomally and as a topic of general scientific interest, by the discoveries in 1974 by F. H. Allen, S. M. Fu and their colleagues that the genes coding for Factor B and C2 are linked to *HLA*. This had been fore-

shadowed in 1973 by the work of P. Demant and colleagues showing that the Ss protein, coded within the *H-2* region of mice, was a complement component, subsequently shown by several groups of workers to be C4.

The complement system consists of at least 18 proteins, including pro-enzymes and inhibitors, whose activity is usually triggered by the binding of antibody to antigen. It is the major humoral effector system for the elimination of bacteria and viruses in vertebrates and is characterised by complex reaction pathways reminiscent of the clotting, fibrinolysis and kinin systems.

There is now good evidence that three complement components are coded by genes located within the *HLA* region: C2, Factor B and C4. The electrophoretic variants of C4 described by P. Teisberg (Ullevål Hospital, Oslo) show clear *HLA* linkage and both G. Mauff (Hygiene Institute, Cologne) and G. Hauptmann (Institut d'hématologie et de transfusion sanguine, Strasbourg) reported their methods which show the same phenomenon with rather improved resolution. These results confirm the earlier evidence for C4 linkage from studies of a deficient patient's family (C. Rittner, Institute of Forensic Medicine, Bonn). *HLA* linkage is now firmly established for C2 polymorphism (C. Alper, Center for Blood Research, Boston). The less common allele of C2 (2C' in the nomenclature proposed) was reported by T. Meo (Basel Institute for Immunology) to be in strong linkage disequilibrium with *HLA* BW15 and *HLA* CW3.

Alper also demonstrated polymorphism of C8 detected by isoelectric focusing and specific functional detection by haemolytic assay. There are at least three structural variants of C8, two of them common. The locus is not closely linked to *HLA*. Two new families with C8 deficient members were described by N. K. Day (Sloan Kettering Institute, New York) and F. Tedesco (Transplantation, Immunology and Blood Transfusion Service, Milan). In both families, there were totally C8 deficient individuals with different *HLA* types, showing that the deficiency genes also cannot be close to *HLA*. Furthermore it was apparent that there is difficulty in ascertaining the heterozygous deficiency states, since in both families, both parents of the propositi had C8 levels within the normal range. Furthermore Alper reported that members of a deficient family heterozygous for the structural variant could nevertheless have low C8 levels. This may explain the discrepancy between these reports and that of Merritt *et al.* (*Third International Workshop on Human Gene Mapping. Birth Defects XII* (7) 331, The

National Foundation, New York, 1976) which claimed *HLA* linkage for C8 deficiency.

D. Glass (Robert B. Brigham Hospital, Boston) presented a large series of carefully measured cases of heterozygous C2 deficiency. There seems to be a significant association with juvenile rheumatoid arthritis and systemic lupus erythematosus in these patients. J. Soothill (Institute for Child Health, London) and J. Mowbray (St. Mary's Hospital, London) have evidence that there is an increased incidence of heterozygous C2 deficiency in infantile asthma and eczema. However, it was pointed out in discussion that apparently high recombination frequency between C2 and *HLA* observed by Glass is probably due to ascertainment errors inherent in measuring complement levels.

C3, C4, C5 and C8 are known to be composed of more than one polypeptide chain, but in no case is there any evidence that more than one locus is involved in coding for the observed polymorphisms. A possible explanation for this phenomenon is given by preliminary experiments of H. Colten (Children's Hospital Boston) and his colleagues (reported by Alper). They have shown that both C4 and C3 obtained from cell-free synthesis by immunoprecipitation occur as larger than expected chains. Their suggested interpretation of this result is that C3 and C4 (and, by analogy, perhaps C5 and C8) are synthesised as single polypeptide chains which are cleaved before secretion, rather like insulin. Only one cistron will then be involved in coding for the whole molecule and all markers will be alleles, irrespective of the chain on which they are found. Since there are now some 20 variants of C3, all of them apparently alleles, this view has its attractions. Some similar complement components seem to be the products of tandem duplicated genes. This is the case with C2 and Factor B. Both are linked to *HLA* in the same subregion and with no crossovers identified between them. Both are single polypeptide chains, heat labile and form part of a complex C3 splitting enzyme. C6 and C7 are consecutively acting components and are both single polypeptide chains. They show close linkage to each other as demonstrated by allotyping (M. J. Hobart, MRC Group on Mechanisms in Tumour Immunity, Cambridge). Although C3, C4 and C5 are similar, C4 is linked to *HLA* but the other two components are not. If these molecules are the products of related genes, then they have been duplicated by processes other than (or additional to) tandem duplication.

A remarkable case of combined

subtotal deficiency of C6 and C7 was reported by P. J. Lachmann (MRC Group on Mechanisms in Tumour Immunity, Cambridge). The proband is in good health. The deficiencies of both components segregate together in the grandchildren, which is to be expected if the structural genes for both proteins are involved, since they are closely linked. Trace C6 and C7 activity appear in the proband's serum in the same pattern of bands, different from either normal C6 or C7 when separated by isoelectric focusing. An interesting speculation is that this may be the result of a 'Lepore' fusion of C6 and C7 genes.

At times the Workshop veered from the strict limits of complement genetics, Alper and F. S. Rosen (Children's Hospital, Boston) presented evidence that C3 nephritic factor is an IgG, on the basis of functional detection of clonal electrophoretic variants and on the transmission of such a clone across the placenta. A. Ferreira (New York University) described a new C4-binding protein in mice, the molecular association giving the appearance of *H-2* linkage. Since more than half of the known complement components now have genetic markers, new components are needed if healthy growth of the topic is to be maintained! □

Progress in coronaviruses

from David J. Garves

A symposium on Human and Animal Coronaviruses was held at the Agricultural Research Council Institute for Research on Animal Diseases, Compton UK on 24-25 March, 1977, and was organised by Professor A. P. Waterson, Royal Postgraduate Medical School, London, and Dr D. J. Garves, Compton.

THE Coronaviridae comprise a family of morphologically similar viruses that cause a wide variety of diseases in man and other animals. Following the recognition of coronaviruses as a distinct taxonomic group in 1968 (see *Nature* 220, 650), with virus particles having a peripheral halo in negatively stained preparations, the number of viruses classified in the group and our knowledge of their characteristics has greatly increased. There are still large gaps in our understanding of the diagnosis, pathogenesis, structure and serology of this economically and, potentially, medically important group and attempts were made to fill these gaps

at the symposium.

Recent reports of coronavirus-like particles in samples from human and equine enteritis, human nephropathy and feline infectious peritonitis have raised the problem of which criteria should be used to identify a coronavirus. It has been found that coronaviruses are difficult to establish in cell culture and for this reason morphology of the virus particle provides the major distinguishing feature. J. Almeida (Wellcome Research Laboratories) and R. Bingham (Royal (Dick) School of Veterinary Studies, Edinburgh) reported new evidence for the morphology and structure of the internal component of avian infectious bronchitis virus. They showed electron micrographs of virus particles within which flask-shaped structures could be seen, the mouth of the 'flask' appearing to open at the outer membrane of the virus. Whether these structures are present in other coronaviruses and what relation they have to the organisation of the genetic material has yet to be determined.

Recent studies on the polypeptide structures of human and animal coronaviruses have shown that, while the number and size of the structural proteins vary between members of the family, some similar features can be seen. The polypeptide profiles may provide a method to distinguish relationships within the coronaviruses and in this context the apparent similarity between the polyacrylamide gel patterns for avian infectious bronchitis virus (M. R. Macnaughton, Clinical Research Centre, London) and calf diarrhoea coronaviruses (J. Laporte, Thiverval-Grignon, France) was of interest.

The genome of avian and porcine coronaviruses has been shown to comprise single-stranded RNA but whether this has a messenger role, as in oncornaviruses and enteroviruses, or is a complementary strand, as in paramyxoviruses, has not been determined. Our understanding of the strategy of the coronavirus genome is greater, however, following the reports of Macnaughton and D. H. Pocock (ARC, Compton) that avian and porcine coronavirus RNA contains polyadenylic acid tracts. This evidence strongly suggests that the RNA has a messenger function and is yet another feature, together with virion morphology and the genome size, that coronaviruses have in common with the RNA tumour viruses. Bingham reported, however, that attempts to detect a reverse transcriptase in avian infectious bronchitis virus have proved unsuccessful, in line with the evidence from inhibitor studies suggesting that coronavirus replication does not pro-

ceed by way of DNA.

D. J. Alexander (Central Veterinary Laboratory, Weybridge) reported on the finding of long term infection of chickens with infectious bronchitis virus and these results, together with the evidence of chronic infection of mice with hepatitis virus and the carrier status of pigs with transmissible gastroenteritis, prompted K. McIntosh (University of Colorado, Denver) to suggest that future work on the human respiratory coronaviruses should consider implications of inapparent, chronic infections. It is possible that Balkan endemic nephropathy may result from such an infection, as K. Apostolov (Royal Postgraduate Medical School, London) reported a possible serological relationship between this disease and a human respiratory coronavirus.

Coronavirus serology is confused at the moment, with cross reactions being detected between human, bovine, murine and porcine viruses. The serological relationship between porcine transmissible gastroenteritis virus and a canine enteric virus is strong and D. J. Reynolds, (Compton) also presented evidence of antibodies to transmissible gastroenteritis in cats. It is possible that the agent in the cat responsible for the very high antibody levels may be associated with feline infectious peritonitis, a possible coronavirus whose morphology and physicochemical properties were presented by A. Osterhaus (Utrecht, Netherlands). The morphology of the purified particles was not characteristic of other coronaviruses and whether this was due to degradation or a different surface projection structure is not known. The agent of feline infectious peritonitis demonstrated the problem caused by the fact that coronavirus identification rests principally on the shape of the surface projection. It was generally agreed that other features including virus structure, the characteristics of the genome and the mode of replication within the cell needed to be determined before any virus could be assigned to the Coronaviridae, although this information is not known for some well accepted coronaviruses. Similarly, more data would be required before any meaningful subdivisions, such as separating the avian from the mammalian members, could be made within the Family.

In the field of coronavirus disease control there seemed to be doubtful correlation between antibody levels in serum and secretions and resistance to infection. It was recommended that more effort should go into investigating cellular and humoral aspects of immunity to diseases caused by coronaviruses. □

articles

Accretion torques in X-ray pulsars

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The character of intrinsic pulse period changes in X-ray pulsars supports the now conventional model for these sources, wherein the X-ray luminosity is derived from the accretion of matter on to a rotating, magnetised compact object, probably a neutron star, and the pulse period changes are caused by its interaction with the accreting matter.

At least nine galactic X-ray sources are known to emit regularly pulsed X rays¹. It is widely believed that the compact objects in these binary X-ray pulsar systems are rotating, magnetised neutron stars². Black holes are eliminated as candidates for these objects because of the existence of periodic pulsations. One or more of the following arguments tend to rule against white dwarfs as the compact objects in at least seven of these systems: (1) the pulse period is too short to be a plausible surface rotation period of a white dwarf (see, e.g. ref. 3); (2) the observed X-ray luminosity is larger than the maximum luminosity of $\sim 10^{35-36}$ erg s⁻¹ that has been predicted by some theoretical models of accreting white dwarfs^{4,5}; or (3) the mass is probably above the Chandrasekhar limiting mass (see, for example, ref. 6).

Another means of distinguishing between white dwarf and neutron star models is through an analysis of the rates of change of the intrinsic pulse periods. As matter is accreted on to the compact star, torques are exerted that will tend to spin it up or down. The time required for accretion torques to spin up a white dwarf will, in general, be considerably longer than for a neutron star. We show here that the observed characteristic spin-up timescales for seven X-ray pulsars strongly support the view that in every source (1) the pulse period reflects the rotation period of a compact object (2), the accretion is mediated by a disk surrounding the compact object and rotating in the same sense, and (3) the compact object is a neutron star rather than a white dwarf.

Theory

In the accretion picture of pulsating X-ray sources, material from an overflow of the critical potential lobe of the companion or from a stellar wind is accreted toward the compact star in nearly Keplerian trajectories. If the net specific angular momentum of the accreting matter is too large to allow direct accretion on to the compact object, then matter will accumulate until an accretion disk forms and permits the outward transport of angular momentum through viscous forces. Ultimately, the matter reaches the Alfvén surface: the surface where the magnetic field of the compact object first dominates the particle dynamics, and where the matter will be forced to nearly co-rotate with the rotating compact star, provided that the circular Keplerian orbital velocity at the Alfvén surface exceeds the corotation velocity Ωr_A . Here, Ω is the magnitude of the vector angular velocity of the compact star and r_A is the characteristic radius of the Alfvén surface. An approximate relation^{7,8} between the Alfvén radius and the parameters of the accreting matter and compact object is given by

$$r_A \approx 3 \times 10^8 (\xi v_t/v_{ff})^{2/7} \left(\frac{\mu}{10^{30} \text{ G cm}^3} \right)^{4/7} \left(\frac{\mathcal{L}}{10^{37} \text{ erg s}^{-1}} \right)^{-2/7} \times \left(\frac{M}{M_\odot} \right)^{1/7} \left(\frac{R}{10^6 \text{ cm}} \right)^{-2/7} \text{ cm} \quad (1)$$

μ , M , R and $\mathcal{L}$ are the magnetic moment, mass, radius and luminosity of the X-ray star, respectively. The quantity ξ represents the fractional solid angle subtended at the compact star by the infalling matter at the Alfvén surface, and v_t/v_{ff} is the ratio of the average radial infall velocity of a particle to its free-fall velocity just outside the Alfvén surface.

In the accretion process, angular momentum is transferred to the X-ray star and its rotation period will change. The X-ray pulsations result from the rotation of the compact object, and the fractional rate of change of the pulse period, $\dot{P}/P = 2\pi/\Omega$, can be expressed as^{7,8}

$$\frac{\dot{P}}{P} = \frac{\dot{M}}{M} \left(\frac{M}{I} \frac{dI}{dM} - \frac{h_a}{h} \right) + \frac{\alpha}{I\Omega} \quad (2)$$

I is the moment of inertia of the compact object, and h_a , h and α are the component of the specific angular momentum parallel to Ω of the material crossing the Alfvén surface, the specific angular momentum of the X-ray star, and the external (viscous and magnetic) torques acting on the X-ray star just above the Alfvén surface, respectively. If the accreting matter counter-rotates with respect to Ω , then $h_a < 0$ and the second term in brackets in equation (2) tends to increase $\dot{P}/P$ (that is, tends to spin down the compact object). The first term in brackets is, in general, small compared to the second term for the case of a white dwarf or neutron star with $r_A \gg R$, provided that an accretion disk exists. The maximum spin-up or spin-down rate will occur when the external torques are small, which is expected if the circular Keplerian orbital velocity at r_A exceeds Ωr_A (ref. 9).

It is instructive to compare the maximum spin-up rate with those measured for the X-ray pulsars. The relation $\dot{P}/P \propto -(M/\dot{M})(h_a/h)$ can be expressed⁸ in terms of the parameters of the compact star and the luminosity:

$$\frac{\dot{P}}{P} \approx -2 \times 10^{-5} \left(\frac{M}{M_\odot} \right)^{-3/2} \left(\frac{R}{10^6 \text{ cm}} \right) \left(\frac{R_g}{10^6 \text{ cm}} \right)^{-2} \times \left(\frac{r_A}{10^8 \text{ cm}} \right)^{1/2} \left(\frac{\mathcal{L}}{10^{37} \text{ erg s}^{-1}} \right) \left(\frac{P}{1 \text{ s}} \right) \text{ yr}^{-1} \quad (3)$$

where R_g is the radius of gyration of the X-ray star. When combined with (1), the relation becomes

$$\frac{\dot{P}}{P} \approx -3 \times 10^{-5} (\xi v_t/v_A)^{1/7} \left(\frac{M}{M_\odot} \right)^{-10/7} \left(\frac{R}{10^6 \text{ cm}} \right)^{6/7}$$

$$\left(\frac{R_g}{10^6 \text{ cm}}\right)^{-2} \left(\frac{\mu}{10^{30} \text{ G cm}^3}\right)^{3/7} \left(\frac{\mathcal{L}}{10^{37} \text{ erg s}^{-1}}\right)^{6/7} \left(\frac{P}{1 \text{ s}}\right) \text{ yr}^{-1} \quad (4)$$

For simplicity, we write this as

$$\frac{\dot{P}}{P} \approx -3 \times 10^{-6} f \left(\frac{P}{1 \text{ s}}\right) \left(\frac{\mathcal{L}}{10^{37} \text{ erg s}^{-1}}\right)^{6/7} \text{ yr}^{-1} \quad (5)$$

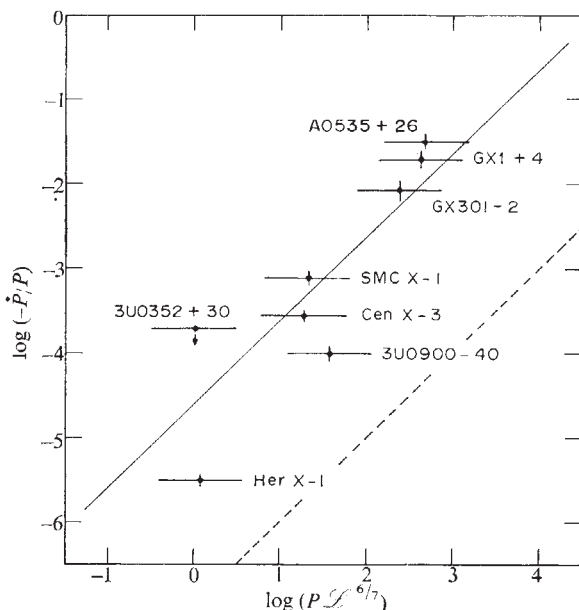
where the dimensionless function, f , is expected to be of order unity for a neutron star and contains parameters that are not yet measurable for most or all of the X-ray pulsar systems.

Observational information

The empirical relation between $\dot{P}/P$ and $(P\mathcal{L}^{6/7})$ is plotted in Fig. 1. The luminosities, pulse periods and spin-up rates for eight X-ray pulsars were taken from the sources indicated in the following paragraphs. In each case, the uncertainty in the distance to the source, the possibility of anisotropic beaming of the X-ray flux, and substantial source variability all contribute to the uncertainty in the luminosity determination. We have assigned to each source luminosity a reasonable but arbitrary uncertainty of a factor of three. For four of the sources (3U0352+30, GX301-2, GX1+4, and A0535+26), the identification of the optical counterpart is probable but not certain; if any of these identifications proves to be erroneous, the corresponding distance estimate would, of course, be invalid.

The pulse period for **Hercules X-1** observed with the SAS-3 satellite in 1975 July was $1.2378082 \pm 0.0000001 \text{ s}$ (ref. 10). This period determination, coupled with Uhuru measurements¹¹ covering the interval 1971 December–1973 March, yield $\dot{P}/P = (-3 \pm 0.5) \times 10^{-6} \text{ yr}^{-1}$. Over shorter time intervals, the value of $\dot{P}/P$ fluctuates and its sign even reverses¹¹. These

Fig. 1 The empirical relation between the fractional rate of change of the pulse period and the parameter (pulse period $\times$ luminosity^{6/7}) for eight binary X-ray pulsars. The units of $\dot{P}/P$, P and $\mathcal{L}$ are yr^{-1} , s and $10^{37} \text{ erg s}^{-1}$, respectively. The solid line is the best fit to a power law with logarithmic slope 1.0. The data point for Her X-1 and the upper limit for 3U0352+30 were excluded from the fit. In all cases, we have assumed that the proposed optical identifications are correct (see text). The good agreement with equation (5) for $f \approx 1$ (see text) lends credence to the presently conventional model of X-ray pulsars as rotating, magnetised, neutron stars that are undergoing accretion. The dashed line is the expected relation for $\sim 1 M_\odot$ white dwarfs (see text).



sporadic intervals of spin-down, together with the small average value of $|\dot{P}/P|$, are indicative of a near balance between spinup and spindown for this source⁹. Hence, external torques are probably important in this system. The theoretical interpretation of the short-term fluctuations in $\dot{P}/P$ has been discussed previously¹². The luminosity of Her X-1, taken from ref. 13 (where the distance is estimated to be in the range 2–6 kpc), is $\sim 1 \times 10^{37} \text{ erg s}^{-1}$. We assume here that a nearly constant X-ray luminosity persists throughout the 35-d cycle of the source (see, e.g., refs 13, 14).

The pulse period for **3U0900-40** was measured with SAS-3 in 1975 June–July to be $P = 282.8916 \pm 0.0002 \text{ s}$ (ref. 6). Ten months later the pulse period measured with SAS-3 was $P = 282.870 \pm 0.004 \text{ s}$. This yields an average value of $\dot{P}/P = (-1.0 \pm 0.3) \times 10^{-4} \text{ yr}^{-1}$. The details of the latter SAS-3 observation will be presented elsewhere. Because only two data points were used to determine $\dot{P}/P$, we cannot estimate the magnitude of short-term fluctuations in this quantity (compare with the discussions of Her X-1 and Cen X-3), and we therefore assign a somewhat larger uncertainty to $\dot{P}/P$ than its formal error. We adopt a value of $\sim 1 \times 10^{36} \text{ erg s}^{-1}$ for the average luminosity of 3U0900-40 (ref. 15).

Ariel V measurements¹⁶ of the **Centaurus X-3** pulse period in 1975 January ($4.83704 \pm 0.00004 \text{ s}$) can be combined with Uhuru data¹⁷ covering 1971 January–1972 December, to yield $\dot{P}/P = (-2.8 \pm 0.4) \times 10^{-4} \text{ yr}^{-1}$. The luminosity is taken to be $\sim 5 \times 10^{37} \text{ erg s}^{-1}$ (ref. 18). Cen X-3 is also observed to undergo brief intervals of spin-down on shorter timescales¹⁷.

The pulse period of **3U0352+30** ($P = 835.6 \text{ s}$) has been measured on at least six separate occasions during a 4-yr interval with the Copernicus¹⁹ and SAS-3 (unpublished SAS-3 data, J. G. Jernigan) satellites, and has remained constant to about 1 part in 1.5×10^3 . It is possible that a somewhat larger secular change in the intrinsic pulse period has been fortuitously cancelled during these observations by orbital motion, but we regard this as highly unlikely. A luminosity of $\sim 4 \times 10^{33} \text{ erg s}^{-1}$ is derived from the inferred distance of $\sim 350 \text{ pc}$ (ref. 20).

The **SMC X-1** pulse period observed²¹ with the SAS-3 satellite in 1976 February was $0.714890 \pm 0.000004 \text{ s}$. This represents a change of 0.0026 s from the pulse period determined from a reanalysis²² of Uhuru data from 1971 June ($P = 0.71748 \pm 0.00026 \text{ s}$). Hence, $\dot{P}/P = (-7.7 \pm 2.0) \times 10^{-4} \text{ yr}^{-1}$, where we again adopt a more conservative uncertainty because only two data points were used in the determination. The average luminosity of SMC X-1 (ref. 21) is taken to be $\sim 5 \times 10^{38} \text{ erg s}^{-1}$.

The X-ray pulsations from **GX301-2** have been studied on five separate occasions by the Ariel V, SAS-3, and OSO-8 satellites during 1975 January–1976 February. In 1975 January the pulse period was $699.3 \pm 0.5 \text{ s}$ (ref. 23). During the interval 1975 July 18–25 the pulse period ranged from 699.9 to 700.5 ($\pm \sim 0.2$) s (ref. 24). By 1975 December the pulse period had decreased to $696.4 \pm 0.4 \text{ s}$ (refs 23, 25) and it was observed to be nearly the same in 1976 January²⁴. Thus, the pulse period remained the same to within $\sim 1 \text{ s}$ for $\sim 0.5 \text{ yr}$ after its discovery, after which it decreased by $\sim 4 \text{ s}$ during the next $\sim 0.5 \text{ yr}$. To explain this change in pulse period by orbital Doppler shifts, a minimum projected orbital velocity of $v_x \sin i \sim 800 \text{ km s}^{-1}$ is required. This source has been identified with the Be star Wray 977 (refs 26, 27); the suggested orbital period is $\sim 20 \text{ d}$ (ref. 28) which, if verified, would yield a mass function of $f(M) \gtrsim 10^3 M_\odot$ for $v_x \sin i \gtrsim 800 \text{ km s}^{-1}$. Hence, it is highly probable that the observed long-term period changes are mainly intrinsic rather than orbital. We conclude that $\dot{P}/P = (-0.8 \pm 0.3) \times 10^{-2} \text{ yr}^{-1}$. The luminosity is $\sim 3 \times 10^{36} \text{ erg s}^{-1}$ for a source distance of $\sim 2 \text{ kpc}$ (ref. 26).

The periodic nature of the X-ray emission from **GX1+4** was discovered in 1970 October during an MIT balloon observation²⁹. The pulse period at that time was $135 \pm 4 \text{ s}$ (W. H. G. Lewin, personal communication). The pulse period was subsequently measured with the Copernicus satellite²³ in 1972

September ($P = 130 \pm 0.4$ s, aliased by the sampling time of the instrument²³), and with the SAS-3 satellite³⁰ in 1975 December ($P = 121.370 \pm 0.005$ s). The pulse period was also measured with the OSO-8 satellite³¹ on two occasions: 1975 September ($P = 122.46 \pm 0.03$ s) and 1976 March ($P \sim 120.0$ s). These data yield an average value of $\dot{P}/P = (-2.0 \pm 0.5) \times 10^{-2} \text{ yr}^{-1}$. The luminosity of this source is estimated³² to be $\sim 4 \times 10^{37} \text{ erg s}^{-1}$, based on the tentative identification of an M giant star³³ at ~ 10 kpc as the optical companion (and on its probable proximity, in any event, to the galactic centre).

When pulsations were first discovered³⁴ from the transient source A0535+26 on 1975 April 28, the pulse period was 104.17 ± 0.09 s (G. K. Skinner, personal communication). The period was determined about 1 month later to be 103.828 s (ref. 35). We attribute this substantial difference to a change in the intrinsic pulse period. If this is the case, then $\dot{P}/P = (-3.5 \pm 0.9) \times 10^{-2} \text{ yr}^{-1}$ during 1975 May. Subsequent smaller changes in the pulse period have been attributed largely to orbital motion³⁶. The source has been tentatively identified with the Bpe star HDE 245770 (ref. 37). If we take the distance of this source to be in the range ~ 1.5 kpc (J. Hutchings, personal communication) to ~ 5 kpc (ref. 37), then the average luminosity during 1976 May was $\sim 6 \times 10^{37} \text{ erg s}^{-1}$.

The quantities $\dot{P}/P$ and $P\dot{\mathcal{L}}^{6/7}$ for the above sources are displayed in Fig. 1. Spin-up is observed in all cases (that is, the average value of $\dot{P}/P$ is negative), indicating that the accreting matter generally rotates in the same sense as the compact object (see equation (2)). A log-log plot of relation (5) has slope 1.0 and an intercept at $\log(-\dot{P}/P) = -4.5 + \log f$. Superimposed on the data points in Fig. 1 is a best-fit straight line with slope 1.0. The data for Her X-1 were excluded in the fit because of the apparent balance between spin-up and spin-down and the resultant possibility that appreciable external torques are present in this source. In view of the probable fluctuations in f from source to source, the fit is quite good. This result strongly indicates that the second term in parentheses in equation (2) dominates the first term, and that accretion disks are therefore present in these sources. In at last two theoretical studies^{38,39}, the existence of an accretion disk in some binary X-ray sources had been called into question.

The measured intercept of the straight line on Fig. 1 is -4.6 ± 0.4 (2σ), in good agreement with equation (5) for $f \simeq 1$. Thus, the observationally determined average value of f is $0.3 \lesssim f_{\text{obs}} \lesssim 2$.

Discussion and conclusions

For the case where the X-ray star is a rotating white dwarf, the value of f is much smaller than for a neutron star. The radius and radius of gyration of a white dwarf are $\sim 10^9$ cm, while the magnetic moment is

$$\mu = 1 \times 10^{33} \left(\frac{B}{10^6 \text{ G}} \right) \left(\frac{R}{10^9 \text{ cm}} \right)^3 \text{ G cm}^3,$$

where B is the surface magnetic field and R is the white dwarf radius. Therefore, we estimate from equation (4) that for a white dwarf $f \sim 0.003$, which is well outside the observationally determined range.

It has been suggested⁴⁰ that the short-period ($P < 10$ s) X-ray pulsars may be white dwarfs that are undergoing accretion and are vibrating in a nonradial mode that is excited by the nuclear burning of the accreted matter. In this model, the pulse period is equal to the vibration period of the white dwarf. The model cannot account for the long-period pulsars ($P > 100$ s), however, since the vibration period of a white dwarf cannot be sufficiently long unless its mass were implausibly small ($\lesssim 0.1 M_{\odot}$). Thus, if the short-period pulsars are actually white dwarfs, then the strong correlation between $\dot{P}/P$ and $P\dot{\mathcal{L}}^{6/7}$ on Fig. 1 must be fortuitous.

The experimentally determined range of values for f is

consistent with the estimated values of neutron star parameters (that is, $M \sim 1 M_{\odot}$, $R_g \sim R \sim 10^6$ cm, and surface magnetic field $B = \mu/R^3 \sim 10^{12}$ G). Because these parameters appear in the function f with widely varying exponents (see equation (4)), the constraints that one can place on the parameters differ greatly. The magnetic field can range from $\sim 10^{11}$ to $\sim 10^{13}$ G and the parameter $(\xi v_t/v_{\text{rf}})$ can range over ~ 4 orders of magnitude without significantly affecting our determination of f . The mass and radius, however, should lie within a factor of ~ 2 of the nominal values for neutron stars suggested above.

The best-fit straight line in Fig. 1 can be used to predict the relationship among pulse period, spinup or spindown rate, and luminosity of any additional X-ray pulsars. For example, if a new X-ray pulsar is discovered and $\dot{P}/P$ is measured, the intrinsic X-ray luminosity of the source can be estimated (unless there are other complications, as in the case of Her X-1) and its distance may then be inferred to within a factor of ~ 2 . Conversely, if the pulse period and X-ray luminosity are known, $|\dot{P}/P|$ may be estimated. We note in this regard that if the existence of 32-min X-ray pulsations in GX17+2 (ref. 19) is confirmed, and if this period represents the rotation period of a neutron star, then $|\dot{P}/P|$ should be $\sim 0.7 \text{ yr}^{-1}$. Thus, at the present time the pulse period of GX17+2 should be about one-half its previously reported value, but the spin-up or spin-down timescale of this source would then be considerably shorter than its known lifetime ($\gtrsim 10$ yr). This result tends to rule against a rotational origin for the pulsations in this source. Similarly, if the 4.8 h period in Cyg X-3 is interpreted⁴¹ as the rotation period of a neutron star, then $|\dot{P}/P|$ should be $\sim 2 \text{ yr}^{-1}$. The measured limit for $|\dot{P}/P|$ in Cyg X-3 is $\lesssim 10^{-5} \text{ yr}^{-1}$ (ref. 42). Thus, it seems very likely that the 4.8-h periodicity is orbital rather than rotational in origin⁴².

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Formation of intense magnetic fields near the surface of the Sun

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Convection concentrates magnetic flux into ropes between granules in the solar photosphere, with average fields of up to 1500 G. The magnetic energy density is locally much greater than the kinetic energy density. Theoretical limits to the amplification of magnetic fields by convection are analysed and related to the observations.

HIGH resolution, ground based observations have recently revealed the presence of very strong, small scale magnetic fields in the solar photosphere^{1,2}. More than 90% of the total magnetic flux, outside pores and sunspots, that emerges from the sun is confined to ropes that are only a few hundred kilometres across¹, with typical fluxes estimated to be less than 5×10^9 Wb (ref. 3). Estimates of the field strength vary from 1,000 to 2,000 G: the only direct measurement of Zeeman splitting, in an infrared line, indicates a field between 1,200 and 1,700 G (ref. 2). These magnetic features are closely associated with the cellular convection pattern seen as photospheric granulation. They can be studied indirectly by observing the solar filigree⁴ and small scale photospheric faculae³. The filigree is composed of bright points and elongated crinkles, which lie in the dark lanes between granules and are moved about by granular convection; moreover, the lifetime of individual features (about 10 min) is similar to the typical lifetime of a granule⁴.

In a highly conducting plasma, magnetic flux is inevitably swept aside by horizontal motions, and concentrated into vertical ropes at the edges of convective cells, especially at the corners where several cells meet. The kinematic amplification of weak magnetic fields is limited by ohmic diffusion but stronger fields exert forces which impede the concentration⁵⁻⁸. There is, however, no adequate theory to describe the dynamic interaction between magnetic fields and convection in the Sun. Traditionally it has been supposed that flux concentration is halted when equipartition between the local magnetic energy density and the kinetic energy density has been achieved. So the field strength B should be limited by the equipartition field $B_e = (\mu \rho U^2)^{1/2}$, where ρ is the density and U the local maximum speed of convection. In the sun B_e rises from about 200 G at the photosphere to 600 G at 1,000 km depth. Hence the equipartition limit is exceeded by the observed magnetic fields.

There is an obvious upper bound to the average field strength within a flux rope, for the field is contained by the external pressure⁹. Clearly the field at the boundary cannot exceed the value $B_p = (2 \mu p)^{1/2}$ that balances the external pressure p when there is no gas pressure within the rope. The field may be stronger on the axis of the tube but in a small flux rope the field is nearly vertical and so the average field strength B cannot appreciably exceed B_p . (If B increases with depth the field observed at the centre of the tube may be larger, owing to the greater transparency associated with the Wilson depression.) At the photosphere $B_p \approx 1,600$ G and B apparently

attains this value. But B_p increases rapidly with depth in the convective zone: at 1,000 km depth $B_p \approx 10^4$ G, at 10,000 km $B_p \approx 4 \times 10^5$ G and at 100,000 km $B_p \approx 10^7$ G.

Thus the small scale magnetic fields pose several theoretical problems. How are they formed and maintained? What limits the field strength? And, in particular, can the field reach values of 10^7 G at the base of the Sun's convective zone?

There are two distinct mechanisms for amplifying the field. The first relies on inhibition of convection by the magnetic field, and the consequent cooling of photospheric gas until thermal and dynamical equilibrium is achieved^{10,11}. In the second, flux is concentrated by the motion until the Lorentz force is strong enough to halt the amplification of the field. Both processes must be included in a full treatment of the dynamic interaction between magnetic fields and convection. We shall show that the equipartition limit is irrelevant and that the maximum field strength that can be produced by flux concentration in the Sun is typically an order of magnitude higher than B_e . Near the photosphere, the field is limited by B_p and cooling is important. Deeper down, the magnetic pressure remains small compared with the gas pressure, though fields of the order 10^4 G can be maintained.

The equipartition limit

The principal argument advanced to support the equipartition limit is that flux concentration can only proceed while the magnetic pressure is less than the dynamic pressure of the motion. If the density and temperature within the flux rope are equal to their mean values in the convecting layer outside it then the magnetic pressure must be contained by an excess gas pressure around the flux tube, and fluctuations in the external pressure should be comparable with $\frac{1}{2} \rho U^2$. Hence $B < B_e$. This argument fails, however, if gas can flow downwards along the lines of force, evacuating the flux tube and reducing the internal pressure. Owing to the rapid increase of density with depth in the Sun, the displaced material can easily be accommodated and so the only limit is set by B_p .

Observations show a downward flow associated with small scale magnetic fields. In the photosphere the greatest measured velocity is 2 km s^{-1} and apparently the velocity decreases with height (ref. 2). The equipartition argument can be adapted for this flow; Parker¹² has investigated various models with fields that are locally enhanced by motion along the lines of force but they are never increased by more than the equipartition field, which is only 400 G. Moreover, for steady flow along a flux tube the downward velocity should increase with height, contrary to the observations. It seems likely that the downflow is a transient effect, associated with the evacuation of the flux tube as it is formed, rather than a permanent feature of an equilibrium configuration.

The thermal mechanism

Biermann's¹⁰ explanation of sunspots invokes the inhibition of convection by a strong magnetic field. Concentration of

magnetic flux reduces the convective energy transport and the photospheric temperature falls since there is less energy to radiate. Cooling proceeds, and the superadiabatic gradient increases, until there is a balance between the reduced energy flux and emission from the photosphere, as well as dynamic equilibrium within the sunspot. This final equilibrium is locally stable³.

This mechanism suggests that a weak uniform field might be thermally unstable: slight condensations would have lower temperatures and pressures, and therefore be liable to further collapse. A field free gas, however, is not liable to sudden condensations. The gas will remain stable unless the magnetic field exceeds some critical value and its effect on convective transport has become significant. The measured magnetic flux through the solar photosphere corresponds to an average field that is too small to produce this instability. The configuration is metastable and the field must be concentrated to rather greater strengths (for example, by supergranular convection) before any thermal instability can proceed.

There is another stabilising effect. The temperature rises beneath any obstacle that blocks the heat flux: hence a local condensation that increases the magnetic field sufficiently to impede convection tends to enhance the thermal as well as the magnetic pressure⁹. At the level where heat flux is diverted convection must produce additional pressures sufficient to contain any resulting increase of the total pressure in the flux concentration. Since the kinetic energy increases with depth, so that B_e reaches about 10^4 G at the base of the convective zone, it is quite possible to form fields of several thousand gauss in flux ropes that extend deep into the Sun.

These arguments apply to the formation of sunspots, which are large compared with the scale of granular convection. For flux ropes that are small compared with granules, the thermal mechanism cannot consistently be separated from the effect of the convective motion. Slender flux tubes are heated laterally¹⁴, with a consequent reduction in the temperature deficit, and it is unlikely that the thermal instability will grow faster than the rate at which flux is swept across the cell. At greater depths, where the flux rope is approximately in thermal equilibrium with its surroundings, the thermal mechanism cannot function.

The normal photospheric temperature of the Sun is about 6,000 K and a small flux tube may be about 500 K cooler than its surroundings¹⁴. If the magnetic pressure nearly balances the external pressure then the flux tube must be almost completely evacuated. Below the surface, lateral heating is less important and the temperature difference can increase. Ropes are formed as flux is brought together by granular convection^{4,13}, giving fields of order B_e , which cause a slight reduction of convective transport in the ropes. The resultant cooling marginally decreases the internal gas pressure. On the axis of a tube, gas is no longer supported by the pressure gradient and therefore falls. The density drops and the tube is squeezed by the external pressure until some equilibrium is reached. A proper description of this process requires a theory of energy transport in the flux tube. We shall instead assume that the density and temperature within the tube adjust themselves to maintain a pressure balance and seek limits to the fields that can be supported by external convection.

Flux concentration by convection

Busse¹⁵ pointed out that laminar convection is dominated by diffusive effects and that the extent to which fields are amplified depends on the relative rates of ohmic, viscous and thermal dissipation. In a Boussinesq fluid (such as a liquid or a shallow layer of gas) the pressure does not enter the equation of state and can be eliminated from the mathematical description of the problem. The equipartition argument, which depends on balancing different contributions to the total pressure, is therefore irrelevant. The governing equations are nonlinear and must be solved on a computer¹⁶. Several simple configurations have been studied systematically in a series of numerical

experiments. In these computations two-dimensional^{17,18} or axisymmetric¹⁹ solutions were obtained for convection between free boundaries in a fluid of electrical conductivity σ and kinematic viscosity ν , in the presence of an imposed vertical magnetic field of average strength B_0 . The general behaviour of these results, which is similar for each configuration, is summarised in Fig. 1.

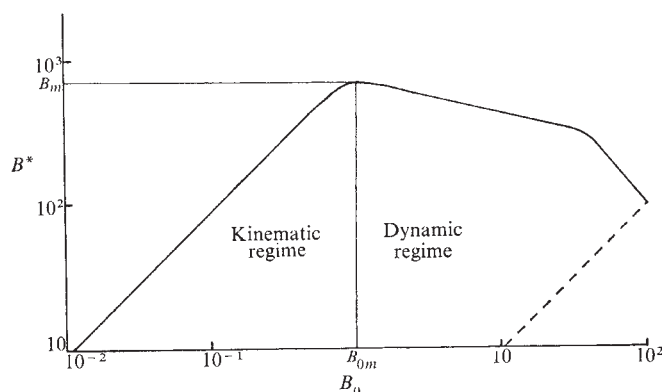


Fig. 1 Amplification of the magnetic field by axisymmetric convection: logarithmic plot of the peak field B^* as a function of the average field B_0 . Magnetic fields are measured in terms of the field B_{0m} at which B^* reaches its maximum value B_m . On the broken line $B^* = B_0$. For this particular run $\nu/\eta = 10$, $B_m/B_{0m} \approx 900$ and the magnetic field suppresses convection for $B_0/B_{0m} \geq 100$.

When the imposed field B_0 is weak the magnetic forces cannot affect the motion. In a steady state the field is amplified kinematically⁶ and the peak field B^* is proportional to B_0 . As B_0 is increased, the Lorentz force becomes significant and the convective velocity is reduced. The amplified field B^* reaches a maximum, B_m , when its dynamical effect is important. In this regime the field is confined to ropes, either at the centre or at the edge of the convective cell, and convection is almost entirely excluded from these ropes. An axisymmetric example is shown in Fig. 2: the flux is concentrated at the centre of the cell, which is stagnant, and the convective eddy occupies a toroidal region that encloses the flux rope. This dynamic regime can be successfully analysed and quantitatively understood in terms of a simple physical model¹⁹. For higher values of B_0 the amplification drops, at first gradually and then more rapidly, and B^* decreases until convection is completely suppressed, whereafter $B^* = B_0$.

In the kinematic regime the work done in containing the magnetic field is small, and the motion is limited by viscous friction. Obviously, kinematic amplification cannot continue after ohmic dissipation has become important. In all the model calculations the transition from the kinematic to the dynamic regime occurs when, or shortly before, the rate of ohmic dissipation in the flux tube becomes comparable with the rate of viscous dissipation in the convecting region. The maximum field B_m can therefore be estimated by equating these two dissipation rates. For higher values of B_0 , well into the dynamic regime, viscous losses are relatively small and the rate of working by the buoyancy force is balanced by work done in keeping the magnetic field within the flux rope. With suitably chosen parameters the field $B^* > B_e$, though global equipartition (between the total magnetic and kinetic energies) occurs only at a value of B_0 greater than that corresponding to B_m .

In three-dimensional flow, flux ropes are formed either at the centre of a cell (as illustrated in Fig. 2) or at a corner where several cells meet. The maximum magnetic field can be estimated from a very simple argument. Consider a cell of depth d and similar horizontal dimensions, and suppose that the flux rope has a radius $\delta \ll d$. The ohmic dissipation per unit volume in the

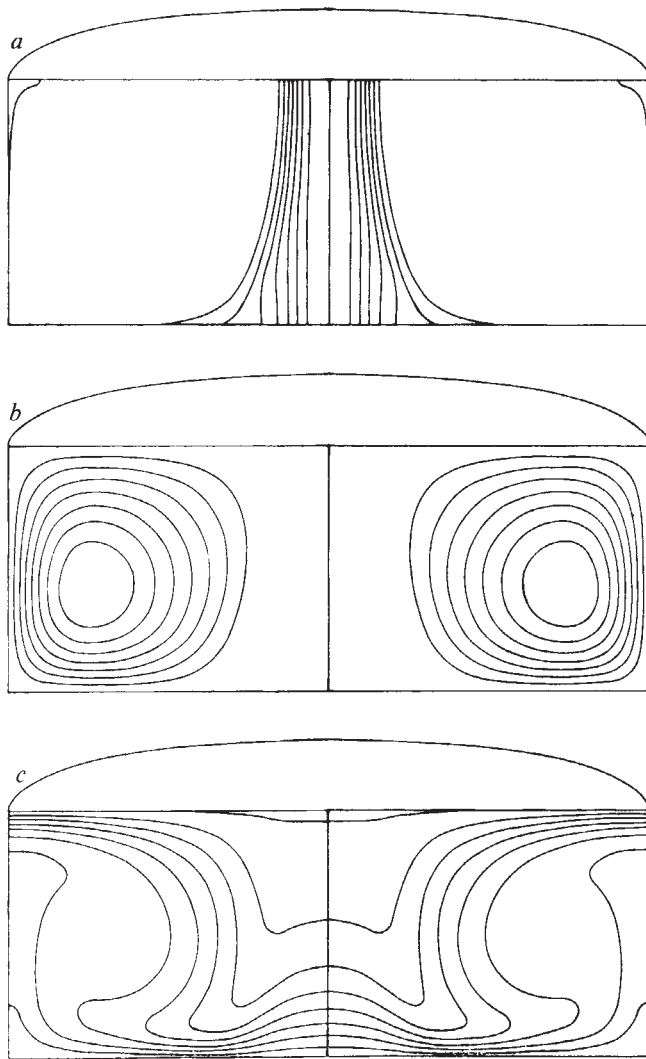


Fig. 2 Thermal convection in a magnetic field: formation of a flux rope in the dynamic regime. Steady solution for axisymmetric flow in a cylindrical cell with free boundaries. *a*, Lines of force of the magnetic field (equally spaced contours of the Stokes flux function); *b*, streamlines (contours of the Stokes stream function); *c*, isotherms, in a meridional plane. The flow is upward around the periphery of the cell and flux is concentrated into an almost stagnant region near the axis.

flux rope is j^2/σ , where j is the current density, and the total ohmic dissipation rate is

$$\left(\frac{j^2}{\sigma}\right) \delta^2 d \sim \left(\frac{B^{*2}}{\mu^2 \delta^2 \sigma}\right) \delta^2 d = \eta \frac{B^{*2} d}{\mu},$$

where the magnetic diffusivity $\eta = (\mu\sigma)^{-1}$. This expression is independent of δ . The total viscous dissipation rate is $(\rho\nu U^2/d^2)d^3 = \rho\nu U^2 d$. The maximum field B_m is reached when these are approximately equal, so that

$$\frac{B_m^2}{B_e^2} = \frac{B_m^2}{\mu\rho U^2} \sim \left(\frac{\nu}{\eta}\right).$$

This ratio becomes arbitrarily large for appropriately chosen diffusivities. The maximum field B_m is only attained for a particular value, B_{0m} , of B_0 . In the kinematic regime, the ratio B^*/B_0 is proportional to the magnetic Reynolds number Ud/η . Hence the transition to a dynamic regime occurs when

$$B_0 \sim B_{0m} \sim \frac{(\eta\nu)^{1/2}}{Ud} B_e.$$

Amplification of magnetic fields in the solar convective zone

In the Sun, convection is not laminar and the pressure cannot be eliminated from the governing equations. Nevertheless, we assume that the field strength cannot exceed the value for which the power needed to contain the flux rope is equal to the rate of turbulent energy dissipation. Observations of granules and supergranules suggest that convective eddies lose their identity after a lifetime τ comparable with the turnover time d/U , as implied by the mixing length theory of convection. Thus the energy dissipation rate in a cell is approximately $\frac{1}{2}\rho U^2 d^3/\tau \sim \rho U^3 d^2$. Although large scale motion is excluded from the flux rope, inefficient small scale convection is still possible within it. The motion is time dependent and mainly vertical, so the field spreads out with an effective diffusivity $\tilde{\eta}$ that is much smaller than Ud (ref. 20). Applying the same argument as before, we find that

$$\frac{B^2}{B_e^2} \sim \frac{d^2}{\tilde{\eta}\tau} \sim \frac{Ud}{\tilde{\eta}}.$$

Thus the ratio of B_m to the equipartition field B_e varies as the square root of the magnetic Reynolds number. (This would follow directly from the previous result if ν were replaced by an eddy diffusivity of order Ud .) The maximum field $B_m \sim (\mu\rho U^3 d/\tilde{\eta})^{1/2}$ then occurs when the average field through the cell is $B_{0m} \sim (\tilde{\eta}/Ud)^{1/2} B_e$.

To find upper bounds for the field concentrated between granules or supergranules we need estimates of the diffusivity $\tilde{\eta}$. Microturbulent velocities in sunspots have magnitudes of about 1 km s^{-1} and horizontal scales of about 10 km (ref. 21): adopting similar values for small scale convective motion in flux ropes between granules, we have $\tilde{\eta} \sim 10^7 \text{ m}^2 \text{ s}^{-1}$. Taking typical values for the granular velocity field ($U = 1 \text{ km s}^{-1}$, $d = 10^3 \text{ km}$, $\rho = 10^{-3} \text{ kg m}^{-3}$, $\tau = 500 \text{ s}$) we then find that $B_e \sim 350 \text{ G}$, while $B_m/B_e \sim 15$; hence $B_m \sim 5,000 \text{ G}$ and is greater than B_p . In practice, therefore, the limit is set by the pressure balancing field B_p , which can be reached by purely kinematic amplification, without the magnetic forces having a significant effect on convection. Now B^* will not reach $1,600 \text{ G}$ if B_0 is less than about 16 G . Hence strong fields should be present only for fluxes $B_0 d^2 \gtrsim 10^9 \text{ Wb}$, which is consistent with Mehlretter's³ estimate of the flux in small scale features.

Magnetic fields are also concentrated at the boundaries of supergranules, which correspond to larger scale and more deep-seated convection ($U = 0.4 \text{ km s}^{-1}$, $d = 1.5 \times 10^4 \text{ km}$, $\rho = 10^{-2} \text{ kg m}^{-3}$, $\tau = 40 \text{ h}$). An estimate of the magnetic diffusivity derived from the decay of long-lived sunspots gives $\tilde{\eta} \approx 2 \times 10^7 \text{ m}^2 \text{ s}^{-1}$ (ref. 20). Hence $B_m/B_e \sim 9$ and, since $B_e \sim 1500 \text{ G}$, $B_m \sim 12,000 \text{ G}$. This crude upper bound is greater than any field that has been observed on the sun but much less than the pressure-balancing field in the same region. The corresponding flux, $B_{0m} d^2 \sim 10^{12} \text{ Wb}$, is comparable to that in a small sunspot.

Deep down in the convective zone the scale of motion is likely to be around 10^5 km . A crude estimate of B_m yields a value of about $70,000 \text{ G}$, corresponding to a flux of about 10^{15} Wb . If the available flux is no more than, say, 10^{14} Wb (the flux through a large sunspot or an active region) then the magnetic field is kinematically amplified to a value around $10,000 \text{ G}$.

We do not suggest that these estimates are precise. But we have shown that fields greater than the equipartition value can be formed where flux is concentrated by the horizontal flow. In the Sun, the convective velocity is outwards from the centres of granules and supergranules and, in a compressible layer, the horizontal velocity is reversed only near the bottom of a convection cell²². Hence concentration is predominantly at the cell boundaries. Some field lines are also carried around within the cells but observations of inner network fields² suggest that the flux involved is relatively small.

Near the photosphere an initially weak field will be concentrated by convection until the thermal instability takes over. The field is limited by the need to maintain pressure balance, and cannot appreciably exceed 1,600 G in a small flux rope. At depths greater than about 1,000 km thermal effects are less important, cooling is slight and flux concentration is limited by diffusion. The maximum field B_m may be an order of magnitude greater than the equipartition field and we expect that flux ropes may have fields of up to about 10^4 G. Similar arguments may be applied to estimate the fields in other stars where magnetic flux is concentrated by convection.

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Discovery of the Hadrynian Polar Track and further study of the Grenville problem

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Palaeomagnetic poles from North America for the period 1,150–650 Myr fall on a simple single great circle polar track—the Hadrynian Track, and the Grenville Loop. This Loop is consistent with Laurentia and Grenvillia having been an integral single plate unit from the onset of remanence blocking (metamorphic cooling) in the Grenville Province.

PALAEOMAGNETIC studies from the Grenville Province have yielded palaeomagnetic poles that apparently differ from those observed from Interior Laurentia. The many models proposed to explain this discrepancy fall into two classes: the two-plate model^{1–6}, and the one-plate model^{4,5,7–10}. On the two-plate model, it is considered that the north-trending Grenville Track records the gradual convergence of a separate Grenville plate towards Laurentia. Difficulties with the two-plate model are: (1) the magnetisations which are all post-orogenic were reset at the maximum separation of the two regions, the collision itself apparently produced barely any detectable reheating, (2) the lack of evidence of a suture zone, and (3) the presence of pre-orogenic geological units which cross the Grenville Front and can be recognised as far as 100 km into the Grenville Province. On the one-plate model, the Grenville Track is incorporated into the North American polar wander path by means of a so-called Grenville Loop. The difficulty of this model is in establishing the sense and time calibration of this Loop. Both counter-clockwise¹⁰ and clockwise^{4,5,7–9} loops have been proposed. Establishing the age sequence of the Grenville Track is clearly of major importance. In comparison with the radiometric evidence, the ages assigned to Grenville Loops seem to be either too old^{7,8} (1,400–1,250 Myr), or too young^{4,5,9} (800–600 Myr). In addition, some of the reported Grenville poles which do not fall on the so-called Grenville Track (Fig. 2) have not been satisfactorily accommodated by any of the proposed one- or two-plate models.

We present here a polar wander path for the period 1150–670 Myr (Figs 1–3) which uses all the presently available North American palaeomagnetic data. A portion of the path forms a

Grenville Loop which incorporates all of the Grenville poles (including a north-trending Grenville Track). It also contains some non-Grenville poles. The age assignment for this loop (1,050–950 Myr) is consistent with radiometric evidence. The latter portion of the polar path (950–670 Myr) follows an almost great circle path (Figs 2 and 3) from close to the Equator at 180°E, over the present geographic North Pole, and down to the Equator again close to 0°E. During all portions of this path the average drift rate relative to the pole is 8 cm yr⁻¹, a much more conservative figure than the drift rates required by the previously proposed one-plate models.

Data interpretation criteria

For the construction of this path some initial interpretations are questioned, and new interpretations are presented. In our opinion it is difficult in any study of igneous, metamorphic or sedimentary rocks to show indisputable evidence of an initial (primary) magnetisation. Only a positive contact test provides evidence of a single simple thermo-remanent magnetisation (TRM). In all other cases, elucidation of the sequence of remanence acquisition can only possibly be achieved by detailed laboratory experimentation. For igneous and metamorphic rocks extensive alternating field (a.f.) and thermal remanence cleaning is obligatory; a.f. cleaning alone is inadequate to identify the remanence carrier (for example, magnetite or haematite). Thermal experiments provide the respective blocking temperature spectra, and it may then be possible, using vector analysis, to establish the magnetisation sequence. This still remains hazardous unless it can be shown that both haematite and magnetite remanences are the result of a single cooling event (TRM). Chemical remanence (CRM) acquisition at low or intermediate temperatures, which is probably commonplace, can quite easily produce haematite remanence with high blocking temperature and high coercive force characteristics, but which is of secondary origin. For sedimentary rocks, especially red beds, thermal experiments alone are insufficient for unravelling complex magnetisation sequences; chemical leaching must also be performed¹¹. A.f. experiments are not obligatory but are considered extremely

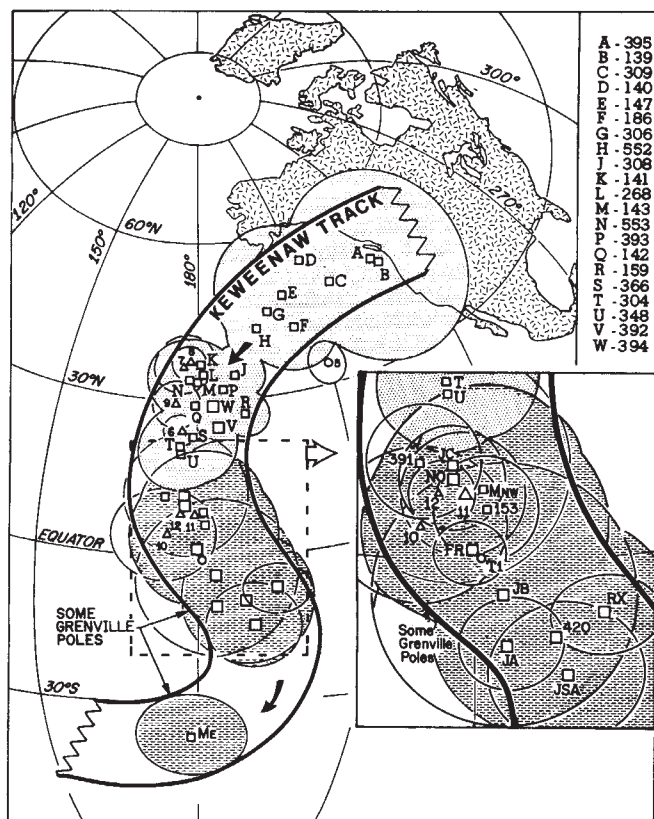


Fig. 1 Polar path for the interval $-1,150$ to $-1,000$ Myr relative to North America. Inset shows detail of the descending portion of the Grenville Loop. Poles A $\rightarrow$ W and those with three digits are listed by their Ottawa Catalogue number²⁵; Δ , poles (enumerated 5–12) from sequential strata in the Grand Canyon Supergroup¹²; all other poles catalogued by letters are referenced in the text. $\square$, Site unit weight; $\circ$, sample unit weight. Approximate error ovals (95%) for the Keweenaw and Grenville data are represented respectively by the dotted and horizontally hatched clouds, and plotted individually for other results. Lambert equal area projection centred on 180°E , 30°N .

valuable. These requirements might seem stringent, but to understand complex geological processes, palaeomagnetic data of the highest quality possible are required. Applying these criteria to this data set, some poles can be regarded as key reference poles (KRP), shown as the larger symbols in Figs 1–3, and discussed in the detailed formulation of our polar path.

The Grenville Loop

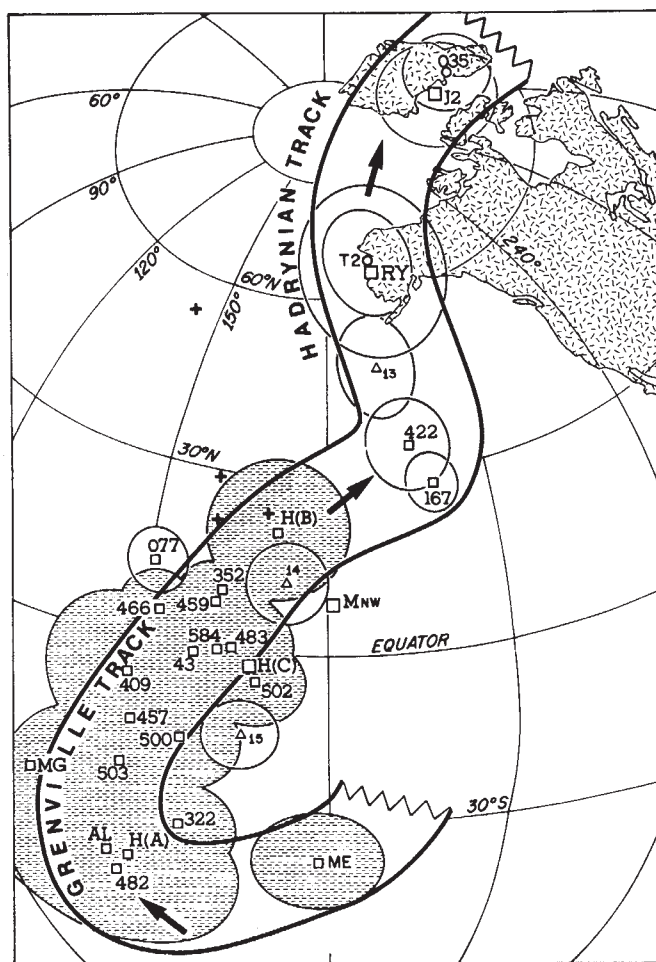
The downward portion of the Keweenaw Track (Fig. 1), which has been established for a few years, is based on a number of KRPs from the Keweenaw volcanic sequences, for example, the Portage Lake Lavas (pole 492) is the mean of several studies. This trend is confirmed by eight poles (5–12) from a measured stratigraphic sequence in the Grand Canyon Supergroup¹². Pole 11 near the equator from the Cardenas Lavas with a Rb/Sr isochron age of $1,090 \pm 70$ Myr (ref. 13) is not significantly different from pole 391 (the Rama diabase)²⁶ suggesting consanguinity of these intrusive and extrusive units of the Grand Canyon Supergroup.

Extension of the polar path southwards over the equator is based on the evidence of four new poles; the Nonesuch Shale (NO) (ref. 14), the Freda Sandstone (FR) (ref. 14), the Rapitan Group (RX) (ref. 15), and the Jacobsville Formation (JC $\rightarrow$ JB $\rightarrow$ JA $\rightarrow$ JSA) (ref. 16). All these results were obtained after extensive chemical, thermal and a.f. experimentation. The Nonesuch and Freda poles sampled over a 900-m section indicate a southward trend. Pole RX from the Rapitan Group is the direction most persistent after chemical leaching. The

Jacobsville was sampled over a lateral distance of 350 km in three areas: Sault Ste Marie (C), Marquette (B) and the Keweenaw Peninsula (A). Although there is no direct stratigraphic control over the relative positions of these three areas, isopach maps¹⁷ indicate the age sequence should be C $\rightarrow$ A. The pole JSA obtained from nine sites (including a field reversal) brings the polar path to 15°S in the descending portion of our Grenville Loop. It is most interesting that the previously underemployed pole 420 from the Shabogamo Gabbro⁸ near the Grenville Front falls between poles RX and JA. From this downward-trending limb the polar path is connected to the southern end of the Grenville Track through the Grenville pole Me (Mealy Mountain—east component)⁸.

The north-trending Grenville Track is based on detailed studies of polyphase magnetisations^{3–6, 7–8}. In studies with two-phase magnetisations the remanence component with lower blocking temperature, lower coercive force characteristics (Grenville Group B poles) plot to the north of the higher blocking temperature, higher coercive force magnetisations (the Grenville Group A poles). Assuming that these magnetisations record a simple slow cooling exhumation TCRM–TRM, the designated age sequence then would be from south to north. A TCRM thermochemical remanent magnetisation, is to be expected as chemical changes are bound to occur during any extreme reheating (metamorphism) event. Support for this simple TRM hypothesis is provided by the record of A group poles carried by both magnetite and haematite in studies from the Magnetawan metasediments¹⁰, and the Haliburton intrusives⁶.

Fig. 2 Polar path relative to North America for the interval $-1,000$ to -850 Myr. The poles are labelled as before. $\square$, Site unit weight; $\circ$, sample unit weight. Approximate error ovals (95%) for the Grenville data are represented by the horizontally hatched cloud, and plotted individually for other results. Lambert equal area projection centred on 180°E , 30°N .



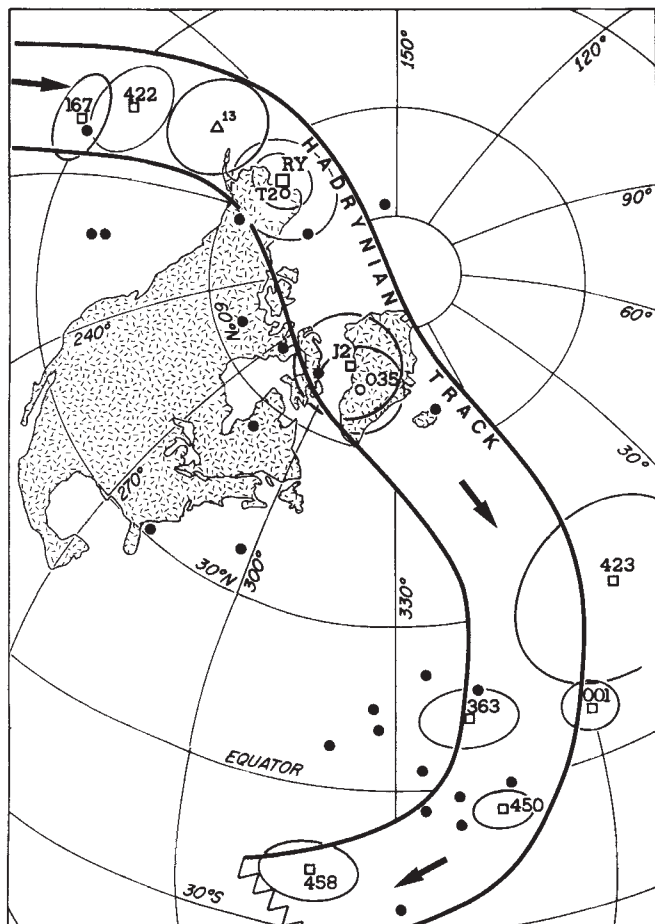


Fig. 3 Polar path relative to North America for the interval -950 to -670 Myr. The poles are labelled as in Fig. 1. □, Site unit weight; ○, sample unit weight; ●, Grenville Province dyke poles; △, Grand Canyon pole (13). Solid plots indicate individual site mean poles from the post-metamorphic Grenville Province dykes²³. Approximate error ovals are plotted individually. Lambert equal area projection centred on 330°E, 60°N.

Detailed experimental work on the Allard Lake anorthosite (AL) provides particularly good evidence for a simple metamorphic TRM¹⁹. Only one direction was found but both polarities are present; normal carried by magnetite, and reverse by haemo-ilmenite. Where dual magnetisations of differing remanence directions are ascribed to separate magnetite and haematite remanences, the evidence for the northward shift is less convincing because of the possibility of chemical remanence overprinting (for example, poles 482 and 483 from the Morin anorthosite¹⁸). By comparison with the Allard Lake result (AL) it is most probable that pole 482 represents a TCRM.

On this polar scheme, poles Me and 420 from or adjacent to the eastern Grenville Province predate poles from the western Grenville Province which define the Grenville Track; this indicates that uplift cooling in the east predated cooling in the west as previously suggested²⁰. The Shabogamo Gabbro (pole 420) outcrops outside the Grenville Province, however, and may belong to an earlier portion of the Laurentian Precambrian polar path. Pole Mnw obtained from a.f. experiments alone from the eastern Grenville is ambiguous; it may belong to the descending Keweenaw Track (Fig. 1) or the ascending Grenville Track (Fig. 2). Owing to lack of thermal cleaning, this cannot be resolved at present.

The Hadrynian Track

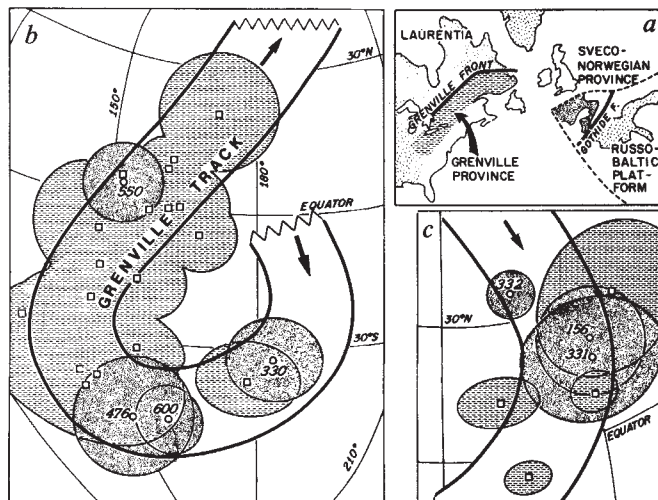
From about 950 Myr at 180°E on the Equator the polar path moves northwards over the present geographic north pole and

then southwards to the 675 Myr Franklin KRP (450) near the Equator at 0°E. Because of the age limits on this path, we suggest the name Hadrynian Track is most appropriate.

Transition from the Grenville Loop to the north-trending Hadrynian Track is suggested by two studies, which also confirm our one-plate model. Firstly, contrary to the original suggestion⁶, the magnetisation sequence A→C→B from the Grenville Province Haliburton intrusives favours a one-plate model. On a two-plate model pole (H)B lies well north of the assumed polar juncture (collision) which supposedly took place near the Equator. Also, poles 13-15 from the upper part of the Grand Canyon Suite¹² are consistent with a one-plate model, and a northward-trending Hadrynian Track if the accepted magnetisation sequence is 15→14→13. No chemical leaching was attempted on the ferruginous units 14 and 13, and it is questionable whether the initial magnetisation has been effectively isolated. Furthermore, studies of the probably correlative and contemporaneous haematite-rich Rapitan Group¹⁵ and underlying Little Dal Lava from the Mackenzie Mountains N.W.T. indicate that secondary haematite overprints with similar poles are quite common (for example, pole RY). On the upward trend the Hadrynian Track picks up poles 422 (Stoer Group) and 167 (El Paso) both of which are dated at approximately 950 Myr, and the secondary site mean poles of the Pikes Peak Granite²¹ (crosses).

For the high latitude portion of the Hadrynian Track the KRPs are RY (Rapitan Group) and J2 (Jacobsville Formation). Both these magnetisations have high blocking temperature and remanent coercive force spectra. Chemical experiments on the Rapitan indicate that RY most probably postdates RX. J2 is a CRM superimposed upon the JA, JB and JC magnetisations. Supporting evidence for the track over the pole is provided by poles Orienta 2 (T2) and Chequamegon (035) (ref. 22) which plot near the RY and J2 poles, respectively. The Orienta 1 (T1) and Orienta 2 (T2) have great similarity with JA and J2. Site poles from Grenville Province diabase dykes²³ which postdate the Grenville metamorphic episode can be divided into two groups, one tightly grouped about the Franklin pole (450), the other group yielding poles which crudely follow the Hadrynian Track. On the downward portion of the polar path, the track passes sequentially through poles from the basal Torridon sandstone (423), the Torridon Group (001), the Fron-

Fig. 4 Comparison of poles from the Sveco-Norwegian and Grenville Provinces. *a*, The proposed reconstruction as discussed in the text, showing the Gothide and Grenville Fronts sub-parallel. *b*, After correction to this reconstruction poles 330, 600, 476 and 550 from the Sveco-Norwegian Province gneisses are not significantly different to poles (hatched cloud) from the Grenville Province. *c*, Poles 332, 156, 331 from late-stage dykes intruding the Sveco-Norwegian Province are consistent with contemporaneous poles (horizontally hatched) after correction to the proposed reconstruction.



tenac dykes (363), and terminates with the Franklin diabase (450) and the Tudor Gabbro (458). Placing of the latter pole on this portion of the track is in accordance with the reported K-Ar isochron age²⁴.

Grenville and Sveco-Norwegian Provinces

The proposed Grenville Loop accommodates all the relevant palaeomagnetic data available including Grenville poles which lie outside the Grenville Track, and the non-Grenville poles which fall close to the Grenville Track, thereby seriously favouring a one-plate model for development of the Grenville Province. Because of the geologic and radiometric similarities of the Sveco-Norwegian Province of the Baltic Shield, it is pertinent to investigate whether palaeomagnetic poles from this region are compatible with the above polar path. Previous comparisons of poles from the Grenville and Sveco-Norwegian Province have explained the residual polar discrepancy after correction to the Bullard refit in terms of transcurrent motion along the line of the Caledonides⁵. This method does not provide an exact polar match; the Grenville and Sveco-Norwegian Tracks are still seen to cross-cut one another. As shown in Fig. 4 an exact match of the poles can be achieved by a 30° clockwise rotation of the Baltic Shield about a Euler pole at 170°E, 40°S after first correcting to the Bullard reconstruction. Poles 330 and 476 (Rogaland basement) and pole 600 from the Farsund intrusion²⁷ plot near the base of the Grenville Loop, while pole 550 (Bamble area)²⁸ plots close to the end of the Grenville Track. Poles from the Hunneadalen dykes (332) and Egersund dolerites (156, 331) which have been dated by K-Ar at approximately 660 Myr are shown to bear the same relationship to the Sveco-Norwegian Province as the Grenville Province diabbases do to the Grenville Province. In this configuration the Gothide Front, which is sub-parallel but not colinear

with the Grenville Front, is seen to form the southern margin of a unified Grenville-Sveco-Norwegian Province. The Grenville Front forms the northern boundary. This reconstruction further confirms our case for an integral single plate unit consisting of the Grenville-Laurentian, and Sveco-Norwegian-Baltic Provinces during the remanence blocking, caused by metamorphic cooling in the Grenville and Sveco-Norwegian Provinces. In conclusion, however, it does in itself pose another fundamental question: what mechanism was responsible for the intense remobilisation of the Grenville Province between 1,050 and 950 Myr?

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letters to nature

Detection of optical pulses from the Vela pulsar

PULSED optical emission has been detected from the Vela pulsar, PSR 0833-45. Double pulses were detected from an area which included Lasker's¹ star M. The pulsed emission has a time-averaged blue magnitude of approximately 25.2 min.

The observations were made on three nights, 24-27 January, 1977, at the f/15 focus of the 3.9 m Anglo-Australian Telescope, Siding Spring, Australia. A twin photometer with two apertures, each 5.0'' arc in diameter, spaced by 17.5'', was used for all observations. Its two photomultipliers had S-20 photocathodes and were used without filters. The signals were fanned out to three experiments which were made as independent as possible.

In the first pulse, counters connected to each photomultiplier were sampled every millisecond by the telescope's instrument computer system, the data recorded on magnetic tape, and

simultaneously binned at the apparent pulsar period for on-line display. The UTC of each sample was established with an error in epoch of ± 1 ms and in frequency of one part in 10^9 using shortwave radio time-signal transmissions. The candidate position was interchanged from one aperture of the photometer to the other at intervals of about 1 h. Pointing and guiding were estimated to be reliable to 1 arc. As a check on our techniques, the Crab pulsar also was observed each night.

In off-line analysis the magnetic tape data were synchronously integrated at the apparent pulsar period in blocks of about 1 h duration. These profiles were then added in the correct phase by computing arrival-times at the solar-system barycentre. Data for the pulsar barycentric period used in this analysis were obtained from the continuing series of pulsar timing observations² at the NASA Deep Space Station, Tidbinbilla, at a frequency of 2295 MHz. Radio observations were made before and after the optical observations.

Table 1 Observations in Vela field

No.	$\alpha(1950)$ h min s	$\delta(1950)$ ° ' ''	Integration time (h)	Description
1	08 33 39.35	-45 00 08.6	6.34	Radio position from ref. 4
2	08 33 39.26	-45 00 11.7	1.85	Position of star M as given in ref. 1
3	08 33 39.35	-45 00 06.6	1.17	2'' arc N of radio position ⁴
4	08 33 39.43	-45 00 13.2	0.33	0.07 s E of the star B2 0.8'' E, 4.6'' S of radio position ⁴

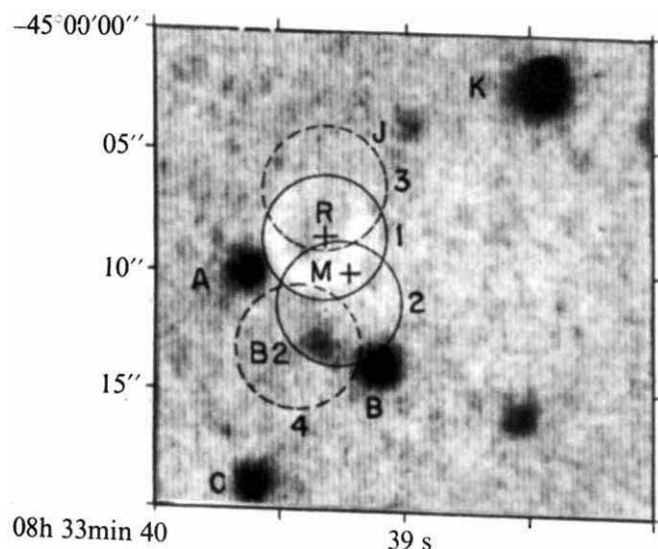


Fig. 1 The field of the Vela Pulsar as it appears, shear distorted, on the TV monitor of the Anglo-Australian Telescope. Circles 1 and 2 enclose the areas of sky where pulses were detected. The radio position (R) of Goss *et al.*⁴ and the position of star M are indicated by crosses. No pulsed light was detected from the areas of sky enclosed by the dashed circles 3 and 4. The white circle enclosing the radio position is a fiducial mark in the TV monitor.

In experiment 2, the data were integrated on-line in a Fabri-Tek signal-averager at the appropriate Doppler-shifted period. The period was generated by a Monsanto frequency synthesiser. The start of each run was initiated by the observatory clock but thereafter the frequency synthesiser ran on its own internal oscillator. The third system fed signal and timing pulses to an analogue tape recorder.

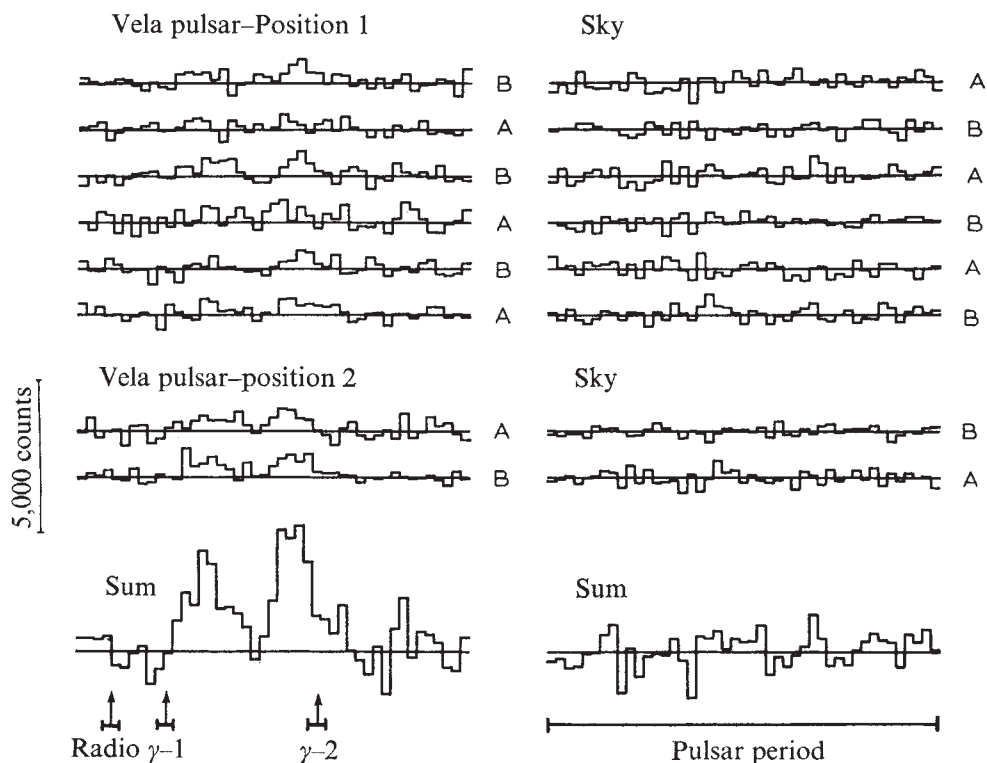
Astrometric measurements made from an AAT prime focus plate of stars in the Vela field agreed with those of Lasker *et al.*³, for their stars A, B, C, F, G and K, but disagreed with the positions given by Lasker¹ for stars A and M. Our position (1950.0) for star A is $\alpha = 08\text{ h } 33\text{ min } 39.68\text{ s} \pm 0.03\text{ s}$, $\delta =$

$-45^\circ 00' 09.9'' \pm 0.3''$, and for star M (measured from the photograph by Lasker¹), $\alpha = 08\text{ h } 33\text{ min } 39.22\text{ s} \pm 0.03\text{ s}$, $\delta = -45^\circ 00' 10.1'' \pm 0.33''$.

A total of 10 h observation was obtained at the four positions listed in Table 1 and shown in Fig. 1. Pulses were observed only at the radio position⁴, which has errors of $\Delta\alpha = 0.04\text{ s}$, $\Delta\delta = 0.8''$, and at position 2. Figure 1 shows, with our measurement of its position, that Lasker's star M was within the overlap of the apertures for both of these. Light curves for the observations are shown in Fig. 2, together with the curve obtained by summing the data from the two positions. Figure 3 shows a single curve from the multi-channel analyser system, which gives results in close agreement. The phase of radio pulse (corrected for delay due to dispersion) and γ -ray pulses⁵ relative to the optical pulse are also indicated in Fig. 2. Unlike the Crab pulsar, the Vela pulsar emissions in different wavelength regimes are at different phases. The optical pulse shape is double peaked with a component separation of $22 \pm 2\text{ ms}$. The second pulse is stronger, but further observations are required to investigate detailed pulse structure. The radio pulse which is essentially single-peaked, is emitted $20 \pm 2\text{ ms}$ before the first optical pulse. This places the optical pulses symmetrically between the γ -ray pulses, which have a separation⁵ of 35 ms.

The fact that Lasker's star M was within the aperture at both positions 1 and 2 where pulses were detected allows the possibility that this is the pulsar. Some support for this is given by the slightly greater intensity of the observed pulses at position 2 for which the star M is closer to the centre of the aperture. (The seeing during the observations was generally between $1''$ and $2''$.) Lasker finds that star M has a B-magnitude of 23.7 with an assumed error of ± 0.5 . We estimate the time-averaged blue magnitude of the pulsed emission to be 25.2 with the same assumed error. This estimate is based on comparison with the Crab pulsar⁶, which has a B-magnitude of 17.0. We assume that the Vela pulsar was wholly within our diaphragm for all observations at positions 1 and 2 and that it has the same colour as the Crab pulsar. Measurements of the B sky brightness at the South Celestial Pole by the UK Schmidt Telescope Unit on the three nights of our observations imply a similar magnitude for the Vela pulsar. At face value,

Fig. 2 Phase plots of the light curves of the pulsar (left) and simultaneous sky noise (right) as seen through the twin apertures A and B. Data have been binned to 2 ms resolution. Position 1 is centred on the radio position⁴, and 2 on Lasker's position¹ for star M. Phases of emission of the radio pulse² with respect to the optical pulses, and of the two γ -ray pulses⁵ with respect to the radio pulse are indicated at the foot of the figure. The indicated levels of the background were determined by averaging the baseline regions outside the optical pulses. For the summed pulsar profile the background was 334,800 photocounts per 2 ms bin. The corresponding level of the sky channel was 319,300.



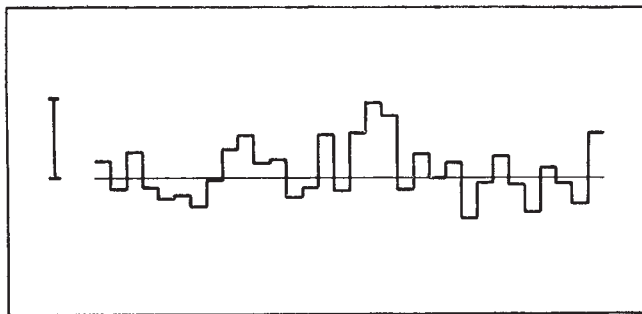


Fig. 3 The first hour long run with the second experiment, on the radio position, displayed in 32 bins. In common with the first experiment every comparable run shows the double peak, subject to photon statistics. The vertical bar is twice the Poisson dispersion.

and assuming conventional values for the distances⁷, these magnitudes imply that the dependence of pulsed luminosity on period for optical pulsars follows a $P^{-1.2}$ law (compare with ref. 8).

Further observations are required to determine whether or not star M is the pulsar and, if so, what fraction of its light is pulsed.

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Search for γ -ray bursts with coincident balloon flights

WE report on an experiment to search for cosmic γ -ray bursts of the type discovered by Klebesadel *et al.*¹, but of smaller size and of sufficient frequency of occurrence to be detected during a 1-d observation program. Two similar detectors, successfully balloon-borne from launch sites in South Dakota and Texas, achieved about 20 h of simultaneous operation at several millibars atmospheric depth, with continuous separation of over 1,500 km on 10–11 May 1975. Fluctuations of the counting rates of >150 keV photons with temporal structures from microseconds to several minutes were compared in order to detect coincident or

associated responses from the two instruments. The results of this experiment can be summarised as follows. First, no coincident γ -ray burst events were detected. Second, the resulting integral size spectrum of small bursts, from this and from all other searches, remains a spectrum of upper limits, consistent with an extrapolation of the size spectrum of the largest known bursts, fitting a power law of index -1.5 . Third, a curious effect was found which can be described as consisting of associated, but not coincident, counting-rate increases of photons of energy >150 keV. This phenomenon undoubtedly presents a background, event-confusion problem for any single γ -ray burst instrument, placed either on balloons or on satellites which orbit the Earth beneath the trapped radiation.

This experiment was designed to investigate the possibility that cosmic γ -ray bursts could be detected in the size region of 10^{-7} to several times 10^{-6} erg cm⁻², below the apparent bend in the size spectrum of Vela events as described by Strong and Klebesadel². It has generally been assumed that the observed bend could be due to instrumental effects^{3–5} (because the detector thresholds do not produce a sharp cutoff in event selection, due to the widely varying temporal structures of the bursts). An intrinsic bend in the true size spectrum, however, would be of great interest. A plot of $N(>S)$, the number of events of size greater than S , as a function of event size S , would vary as $S^{-1.5}$ for an extended volume of source objects positioned essentially isotropically, but as S^{-1} for a disk-shaped region and as $S^{-0.5}$ for a one dimensional source region. Thus, the shape of the observed size spectrum not only could indicate a galactic structure in the γ -ray burst source pattern, but also might directly calibrate the intrinsic source strength distribution from the known galactic dimensions.

Our first experiment to search for small γ -ray bursts was the balloon-flight of a single large detector in May 1974—a number of candidate events were found, having sizes consistent with -1.5 index power-law extrapolation, but which could not be established as true γ -ray bursts without confirmation from another detector^{3,6}.

To obtain a more definite signature for cosmic γ -ray bursts, the dual balloon experiment described here was carried out in 1975. Two similar detectors were flown simultaneously with adequate geographical separation to avoid local cosmic-ray or magnetospherically induced coincident responses. One balloon was launched at 0145 UT on 10 May from Palestine, Texas and floated until about 0400 UT on 11 May. The other balloon was launched about 0340 UT on 10 May from Sioux Falls, South Dakota and floated until 2125 UT on 11 May. The distance between the balloons was always greater than the distance between the launching stations, which is about 1,300 km. The total time of simultaneous float above 6.5 mbar residual atmospheric pressure was about 18 h, most of which was above 3.5 mbar depth.

The detector in each instrument consisted basically of a plastic scintillator 8,900 cm² in area and 5 cm thick, viewed by two 5 inch PM tubes in coincidence. The absolute energy threshold was at ≈ 150 keV, although calibration with radioactive sources showed that the average effective threshold was nearly twice this figure. Particles were excluded by a second, anticoincidence threshold set at 2.5 MeV. In each instrument a time interval analyser (TIA) (ref. 7) was used, measuring the time interval ΔT between each pair of successive photon counts. Thus, rapid, short count-rate increases (fast bursts) could be evident in a rate against ΔT histogram as bumps in the region of small ΔT , well separated from the main, Poisson distribution of background γ -ray counts. This made possible a search for temporal structures in counting rates from the 40-ns region continuously to the several hundred millisecond region, with longer structures evident from the use of the total counting rate histogram. The advantage of this system over

the conventional counting rate histogram scheme is that orders of magnitude lower bit-rate telemetry can be used. Absolute time coincidences between the two detectors would have been attainable to 72 ms resolution, except that an electronic problem resulted in an actual accuracy of only 1 s. Therefore, coincidences of increases of less than 1 s duration could only be inferred from their likelihood of occurrence in coincident data samples.

The data analysis showed that indeed non-Poisson counting rate excursions were detected with time bases from the microsecond region to the 1-min region. These could be due to local background such as cascade showers, neutron and cosmic-ray interactions and induced radioactivity, and to magnetospheric effects. A phenomenological data treatment was therefore developed, consisting of plots of the number of fluctuations against size in standard deviations, against time base on a logarithmic scale. For each of the two instruments, a smooth, three-dimensional distribution was found to contain only one bump, other than the background distribution having a maximum near the origin. In each case this extra population consisted

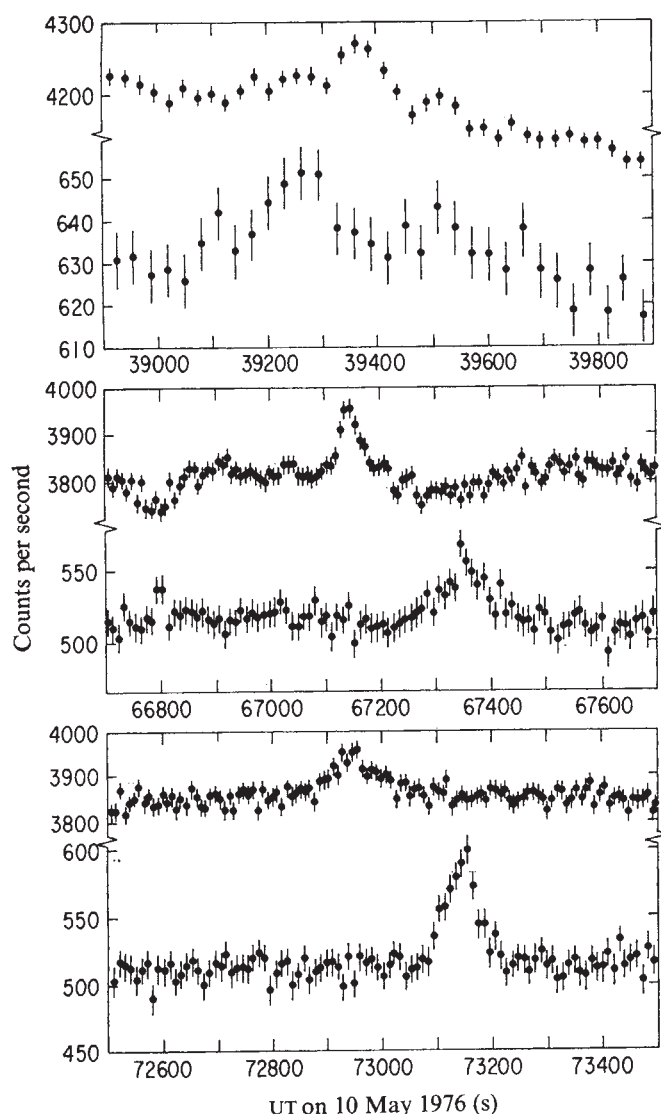


Fig. 1 Counting rate increases exhibited by the γ -ray counters in three occasions. In each record Sioux Falls data are uppermost with Palestine data below. The lack of simultaneity of the events in each case disproves cosmic origin; the fact that the pairs of increases are always separated by a short time delay relative to the time between their occurrence argues for a magnetospheric origin. Such transient increases present a background problem for near-Earth γ -ray burst detectors.

of very long, one half to several minute, counting rate increases of many standard deviations value. No extra population was found in the 0.1–20 s region where all known γ -ray bursts occur. All increases of over a few standard deviations from each instrument of any time character from microseconds to minutes were compared, however, to search for correlated increases from the two detectors. The results were that, except for those expected on a random coincidence basis, none occurred other than the very long time-base population found with the plots, as described above.

Time histories of the most significant counting rate increases are plotted in Fig. 1a–c. (The sensitivities of the two instruments are not the same, but, due to a minor malfunction, the rates of Palestine instrument are somewhat less, and are switched off for 5 s out of each 10 s.) If these increases were γ -ray bursts, assuming the spectrum found typical of longer events⁸, their energy content would be around 10^{-5} erg cm^{-2} each. They are clearly not coincident, however. The light travel time between the two detectors is only 5 ms, and yet the temporal separation is many tens of second. The increases are surely associated, however, since there are only several of these events in either tabulation of single counting rate histograms within the 18 h. Thus, the probability is negligible that each pair should fall within a few minutes separation on a random basis. One explanation of this phenomenon may lie in ionospheric or magnetospheric activity with a slowly travelling disturbance centre. Artificial sources are a less likely explanation. We have checked the VLF receiving records of the Naval Observatory in Washington, D.C. Records were available for the VLF stations WLK, Jim Creek, California, and NBA, Balboa, Canal Zone, and for the Omega stations Trinidad and LeMoure, North Dakota. None of these records show any disturbance during the day of 10 May during which three of our events occurred. The responsible electron fluxes would have to be small, less than one per cm^2 , such that, if magnetospheric, they lie outside the domain of typically studied trapped radiation phenomena. Such counting rate increases are clearly a danger to any experiment seeking to measure γ -ray bursts without confirmation. In either single balloon flight, these events could have been taken to be exceptionally long γ -ray bursts, were it not for the lack of coincident information in the other. It must be added that one associated event took place near local midnight, so it could not be of solar origin (solar flares would also, of course, be seen as exactly coincident). Thus the need is evident for more sophisticated techniques to search for small γ -ray bursts, a need that applies to low-orbiting Earth satellites instrumentation, as well as to balloon flights.

Figure 2 shows the upper limits to the size spectrum of γ -ray bursts resulting from the analysis of our data. We have included 95% upper limits on the basis that we did not see any actual events in our 1975 flights; the energies where we put our upper limits depend on the time increment used for the burst search. The left mark is the result of a separate 0.1-s search. Since the 0.1-s events are a fairly rare subgroup of events in the total amount of satellite data⁹, we regard the results obtained by balloons to date as inconclusive so far as the slope of the size spectrum is concerned. We feel that this unfortunately remains true when the other balloon data, as plotted on this graph, are included. A recent note¹⁰ indicates our reasons for interpreting the results of another balloon experiment search¹¹ as also consistent with no size spectrum slope change. That note enumerates a number of factors which contribute to rendering a balloon-borne search for bursts less efficient than it may have been intended to be. Our conclusion from this experiment, and from various others^{12–14} is that we need an increase in sensitivity by another order of magnitude to be able to adequately detect small γ -ray bursts. If that

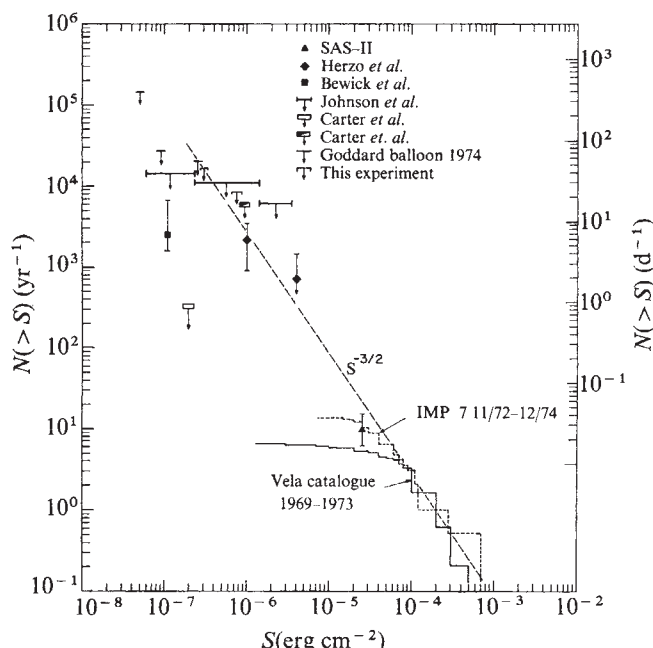


Fig. 2 A plot of the size spectrum of known, large γ -ray bursts and of the various upper limits to the intensity of small bursts, obtained from this and other balloon-borne searches.

can be done, the next step, observing a source direction anisotropy, may be possible.

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Possible γ -ray line from the Crab Nebula

A BALLOON-BORNE γ -ray telescope was flown on 10-11 May 1976 from Alamogordo, New Mexico to search for celestial γ -ray lines in the energy range 100 keV-5.0 MeV. We report here evidence for a line feature from the Crab Nebula at 400 ± 1 keV. Although the counting statistics do not allow us to make an incontestable claim, the fact that it occurs at a reasonable energy to be gravitationally redshifted positron annihilation radiation occurring at the surface of the Crab Pulsar, and in all respects seems to be a real astronomical line, has encouraged us to bring this to the attention of the astronomical community.

The design of the telescope is described in the legend of Fig. 1. A total of 7.4 Crab target and 7.4 Crab background segments were obtained from an altitude of $\sim 122,000$ ft with zenith angles of 12 - 57° . An additional 27 segments were obtained from other astronomical sources. The pointing accuracy of the system was about $\pm 1^\circ$ with the effective entrance aperture increasing slowly with energy from 11° FWHM at 59 keV to 13° FWHM at 1.33 MeV.

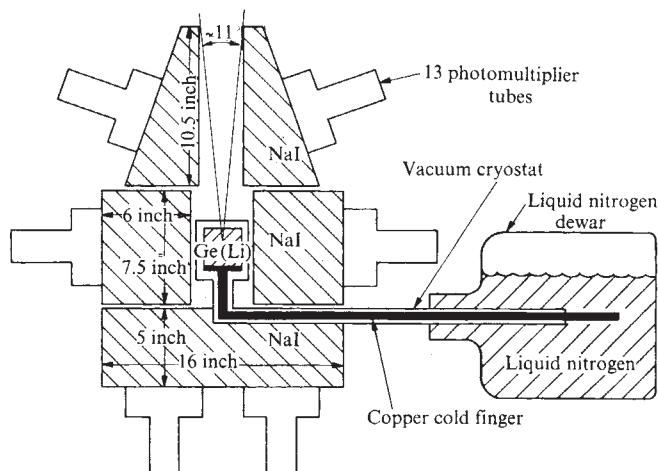


Fig. 1 Schematic diagram of the apparatus. The telescope was designed for optimum sensitivity to lines and contained a 4.70-cm diameter by 6.35-cm long lithium drifted germanium Ge(Li) detector surrounded by 400 pounds of active NaI operated in anticoincidence with the central Ge(Li) detector. The NaI served to collimate the Ge(Li) detector, shield it against atmospheric γ -rays and insure that only full energy events are recorded. Ge(Li) pulses not vetoed by a coincident shield pulse pass through a preamplifier, a shaping amplifier and finally are stored in the onboard memory of a 4096 channel pulse height analyser. The energy resolution of the system below 2 MeV was 3.4 keV FWHM. Data were accumulated in alternate 20-min target-background segments, with the telescope rotated in azimuth 180° but maintained at the same zenith angle for the background measurements.

In Fig. 2 the Crab Nebula difference spectrum extrapolated to the top of the atmosphere is plotted, clearly showing the detection of the X-ray- γ -ray synchrotron continuum at energies below several hundred keV. Also shown is our best fit power law which seems compatible with other recent measurements^{1,2}. Beyond 1 MeV the quality of the continuum data has degenerated to the point that the spectrum becomes

Table 1 Results of 3σ line search of Crab target data

Energy keV	σ	Flux (counts s^{-1})	Tentative identification
139*	29.15	$1.29 \pm 0.04 \times 10^{-1}$	$^{74}\text{Ge} (n, \gamma) ^{75}\text{Ge}$
175	5.53	$1.29 \pm 0.23 \times 10^{-2}$	$^{70}\text{Ge} (n, \gamma) ^{71}\text{Ge}$
198*	40.60	$2.28 \pm 0.06 \times 10^{-1}$	$^{70}\text{Ge} (n, \gamma) ^{71}\text{Ge}$
238	3.52	$6.41 \pm 1.82 \times 10^{-3}$	
356	5.00	$8.64 \pm 1.73 \times 10^{-3}$	$^{56}\text{Fe} (n, \gamma) ^{57}\text{Fe}$
400	4.04	$6.31 \pm 1.56 \times 10^{-3}$	Crab Line
440	4.41	$7.37 \pm 1.67 \times 10^{-3}$	$^{23}\text{Na} (n, n') ^{23}\text{Na}$
473	4.47	$7.47 \pm 1.67 \times 10^{-3}$	$^{23}\text{Na} (n, \gamma) ^{24}\text{Na}$
497	3.41	$5.60 \pm 1.64 \times 10^{-3}$	
570*	17.15	$4.51 \pm 0.26 \times 10^{-2}$	$^{207}\text{Bi} (\text{EC}) ^{207}\text{Pb}$
843	3.49	$4.25 \pm 1.22 \times 10^{-3}$	$^{27}\text{Al} (n, n') ^{27}\text{Al}$
1063*	23.29	$7.01 \pm 0.30 \times 10^{-2}$	$^{207}\text{Bi} (\text{EC}) ^{207}\text{Pb}$
1770*	7.10	$7.21 \pm 1.02 \times 10^{-3}$	$^{207}\text{Bi} (\text{EC}) ^{207}\text{Pb}$

*Lines used in transforming analyser spectra to energy spectra. Apart from the line at 400 keV, all lines appear with comparable statistical significance in the Crab background spectrum and with enhanced significance in the composite spectrum.

consistent with zero net counts from the Crab. Manipulations of the raw data made in obtaining this spectrum deal with the effects of atmospheric attenuation, detector efficiency, system dead time and drifts in the calibration of the energy axis during the course of the flight. Atmospheric attenuation corrections were based on altitude measurements provided us by the Air Force Geophysical Laboratory Balloon Group, using a mean standard atmospheric model confirmed by rocket measurements on flight day. Photopeak detector efficiency as a function of energy was obtained from elaborate Monte Carlo calculations confirmed by laboratory measurements at 14 discrete energies. The high effectiveness of the anticoincidence shield in suppressing the Compton tail and the steepness of the energy spectrum justified the neglect of down-scattered photons. Dead time corrections based on careful laboratory measurements were generally of the order of 20%, due primarily to veto counts in the NaI shield. To correct for system drift in transforming from pulse height analyser channel spectra to energy spectra we first determined the peak channels, in each record, corresponding to five lines at known energies which appeared clearly in all records. Energies corresponding to other channels were then determined by linear interpolation or extrapolation.

We made a careful search of the data for potential sharp line features from the Crab Nebula, by searching both the target and the background data for 5-keV wide bins which contain $> 3\sigma$ excess number of counts over what would be expected based upon the two 10-keV wide bins on either side of the 5-keV wide bin in question. A total of 12 lines were detected which appear in both the target and background data. These are listed in Table 1 with some tentative identifications. Apart from the ^{207}Bi lines, which are from an onboard radio-

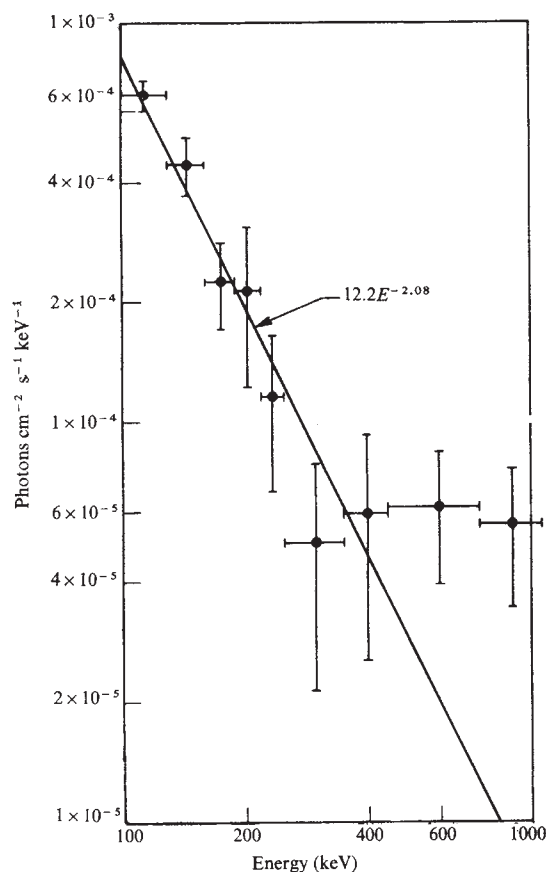


Fig. 2 Energy spectrum of the Crab Nebula's total emission at the top of the atmosphere. The solid line is the power law that best fits the experimental data. The data have been collected into 30-, 100- and 300-keV bins to reduce the statistical scatter of the points.

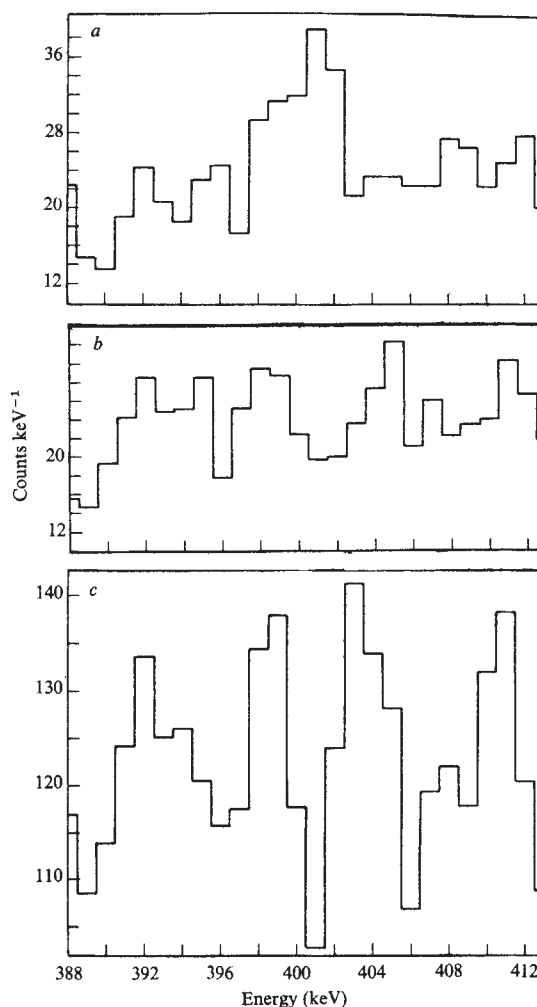


Fig. 3 *a*, Crab target and *b*, Crab background energy spectra in the vicinity of 400 keV; *c*, a composite spectrum of all data less Crab target segments.

active calibration source, most of the remaining lines can be understood in terms of cosmic-ray induced nuclear transitions in the telescope structure and have been seen by other investigators with comparable intensity and width^{3,4}.

In addition to the lines mentioned above, one potential line feature has been detected at 400 ± 1 keV in the target data but not in the background data. Both the Crab target and Crab background spectra in the vicinity of 400 keV are shown in Fig. 3, with a spectrum consisting of a sum of all our data excluding the Crab target segments. These spectra are basically raw data, having been corrected only for drifts in the energy calibration with time. It is believed that the telescope continuum at this energy is dominated by leakage of the atmospheric γ -ray background through the NaI shield. The fact that the feature appears only in the Crab target spectrum is taken as strong evidence that it is not a telescope artefact. It is also important that the line is evident in most of the target segments. The feature represents a 4.0σ deviation above the telescope continuum as determined from the 387.5–397.5 and 402.5–412.5 keV energy bins of the target spectrum. Although the above method was originally used, there are many other valid ways to search the data for lines, each yielding a slightly different level of significance for the 400-keV feature, for example, one can vary the width of the relevant energy bins, theoretically extrapolate the data to the top of atmosphere before searching for lines, use the Crab background data for continuum subtraction, etc. Using these methods, the level of statistical significance can be made to vary from $\sim 3.3\sigma$

to $\sim 4.2\sigma$. Clearly, the probability that the feature is a statistical accident is not negligible, and definitive proof of its reality must await further experimentation. After correcting for atmospheric attenuation and dead time, the feature in Fig. 3 corresponds to a line flux of $2.24 \pm 0.65 \times 10^{-3}$ photons $\text{s}^{-1} \text{cm}^{-2}$ incident upon the Earth with a width $\lesssim 3$ keV. Such a line flux could have produced a feeble feature in the previously most sensitive search for lines from the Crab Nebula¹ made with an instrument of much poorer energy resolution. The absence of a strong indication of it in these earlier data signals a note of caution in accepting the reality of the present result.

Finally, it is interesting to consider a possible physical origin for the feature. Several mechanisms exist for generating positrons at or above the surface of the Crab neutron star^{5,6}. Positron annihilation in dense gases and solids usually results in the emission of 511 keV photons. Should this occur near the stellar surface, the photons would appear to us gravitationally redshifted. This measurement then determines $Z_{\text{Crab}} = 0.28$ (assuming no other sources of frequency shift). Recent neutron star models^{5,7} can then be used to determine the mass of the Crab yielding $\sim 1.4 M_{\odot}$ which is not unreasonable⁷. For this hypothesis to be correct, $\sim 10^{41}$ positrons s^{-1} must be annihilating into 511 keV photons near the neutron star surface (assuming isotropic radiation) which then reach Earth without significant Compton scattering. A more detailed report of the experiment will be published elsewhere.

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Interpretation of observed cosmic microwave background radiation

THE observed cosmic microwave background radiation, which has a high degree of spatial isotropy ($\Delta T/T \leq 10^{-3}$) and which closely fits a 2.7 K black body spectrum, is generally claimed to be the strongest piece of evidence in support of hot big bang cosmologies by its proponents (for a recent review see ref. 1). Alternative explanations in terms of the integrated effect of a suitable population of extragalactic radio sources²⁻⁶ have been criticised, essentially on the ground that there is no known population of extragalactic objects with a source density sufficient to explain the observed small-scale isotropy of the microwave background⁷. We report here that the 'surface of last-scattering' of the observed microwave background radiation corresponds to the distribution of dust in galaxies or protogalaxies with a temperature ≈ 110 K at the epoch corresponding to $Z \sim 40$, and not to a plasma of temperature $\gtrsim 3,000$ K at an earlier epoch ($Z \gtrsim 1,000$), as given by the canonical model of big bang cosmologies. The claim that this radiation lends strong support to hot big bang cosmologies is without foundation.

Wickramasinghe *et al.*⁸ assumed the existence of dust uniformly distributed in intergalactic space. Absorption and re-emission of radiation from galaxies by these grains then produce the microwave background radiation. This dust must have special geometrical properties to make the metagalaxy up to the Hubble radius optically thick around $\lambda \leq 2,000 \mu\text{m}$, but allowing it to be transparent in the visual range. Based on radar scattering data for thin wires, semiconducting needles (for instance, graphite) with length $l \approx 100\text{--}1,000 \mu\text{m}$ and cross-sectional radius $a \ll l$ are expected to have this effect, as they seem to produce a strong peak in the absorption cross-section around $\lambda \approx 2l$. Also, the required intergalactic dust density of $10^{-34} \text{g cm}^{-3}$ is not incompatible with upper limits set by other methods^{9,10}.

The observation of very distant discrete radio sources down to mm wavelengths presents a serious difficulty for this model. The QSOs with the two largest red shifts (OH 471 at $Z = 3.40$ and OQ 172 at $Z = 3.53$) are at distances from us of $0.90 R_0$ and $0.91 R_0$ respectively (where R_0 is the present Hubble radius). Yet they both indicate a second maximum in their emission spectrum¹¹ at $\lambda \approx 3,000 \mu\text{m}$, where the above model implies an optical depth $\gtrsim 4.5$.

We therefore conclude that the microwave background radiation must be explained not in terms of a coupling between matter and this radiation at the present epoch, but in terms of a coupling in a previous epoch within the framework of an evolutionary cosmology.

Rather than specifying a certain evolutionary cosmology (that is, the 'initial conditions'), let us merely go back in time from the present epoch. If the coupling between the radiation and matter occurred when the radius of the metagalaxy was R , then the common thermal equilibrium temperature of matter and radiation is given by

$$T_B \approx 2.7 (R_0/R) \text{ K}, \quad (1)$$

while the wavelength of maximum radiation is given by

$$\lambda_m \approx 1,800 (R/R_0) \mu\text{m}. \quad (2)$$

Provided the total number of absorbers of the radiation at any given wavelength λ is conserved, the optical depth of the metagalaxy at λ is given

$$\delta(\lambda) = \delta_0(\lambda) (R_0/R)^2 \quad (3)$$

where δ_0 is the optical depth at present. If the absorbers are uniformly distributed in the metagalaxy with a present number density n_0 and cross-section $\alpha(\lambda)$, then

$$\delta_0(\lambda) = \alpha(\lambda) n_0 R_0. \quad (4a)$$

If, however, the absorbers are concentrated in galaxies then

$$\delta_0(\lambda) \approx \delta_g(\lambda) N_{\text{og}} S_g R_0, \quad (4b)$$

where $\delta_g(\lambda)$ and S_g are respectively the average optical depth of a galaxy at λ and its average geometrical cross-section (which are assumed to remain unchanged), and N_{og} is the present number density of galaxies in the metagalaxy.

If the absorbers are uniformly distributed in intergalactic space, one can easily make the metagalaxy optically thick⁸ at epochs given by $R/R_0 \leq 0.1$ with a present dust density $\leq 10^{-36} \text{g cm}^{-3}$, without conflicting with the above observations.

Instead of postulating the existence of an unobserved population of intergalactic dust, however, we will work in terms of the known properties of dust distribution in our own Galaxy. The sources of absorption and re-emission of the radiation in past epochs are then taken to be the dust distributions in dusty spiral galaxies, which we take to be similar to that of ours. The condition needed for thermalisation of the background radiation at any epoch is given by $\delta(\lambda_m) \approx 1$.

We do not know the extinction in our own Galaxy at far infrared wavelengths, but the visual extinction $A_g(\lambda_v)$ parallel to the galactic pole¹² for its entire thickness ≈ 0.5 m. As long

as the grains have a sufficient conductivity (for example, graphite, 'dirty' ice, etc.) their extinction is expected to follow approximately an inverse wavelength dependence for $\lambda \gg 2\pi a$ (where a is the grain radius)^{13,14} and there is some supporting observational evidence¹⁵ in the range $50 \mu\text{m} \leq \lambda \leq 1,000 \mu\text{m}$. Assuming this to be the case, and taking $\lambda_v \approx 0.55 \mu\text{m}$ we get $A_g(\lambda_m) \approx 0.5 \times 0.55 \lambda_m^{-1}$ and a corresponding optical depth $\delta_g(\lambda_m) \approx 0.92 A_g(\lambda_m) \approx 0.25 \lambda_m^{-1}$, which is the optical depth appropriate to our calculation, as the dust is believed to be concentrated in a thin disk of thickness $\leq 200 \text{ pc}$ (ref. 16).

The total population of galaxies in the metagalaxy is also highly uncertain and depends on the highly uncertain value of the deceleration parameter q_0 . Taking the current 'best estimate'¹⁷ of q_0 to be 0.03 and assuming a negligible mass of intergalactic matter, we estimate a metagalactic population of around 2×10^{10} dusty spiral galaxies, giving $N_{og} \approx 1.2 \times 10^{-75}$. Then with $R_0 \approx 1.6 \times 10^{28}$ and $S_g \approx 5 \times 10^{45} \text{ cm}^2$ we get $N_{og} A_g R_0 \approx 0.1$. Substituting these values in (3) and using (2) we get

$$\delta(\lambda_m) \approx 1.4 \times 10^{-5} (R_0/R)^3 \quad (5)$$

whence $\delta(\lambda_m) \approx 1$ when $R_0/R \approx 41$. We conclude therefore that the background radiation was coupled to the galactic dust at this epoch $Z = (R_0/R) - 1 \approx 40$, when they both had the common equilibrium temperature $\approx 110 \text{ K}$. There is no difficulty for any type of hitherto proposed interstellar grain, including H_2O ice, to exist at this temperature.

The epoch of galaxy formation is highly model dependent and uncertain, as is the epoch of dust production. The current best estimates¹⁸ of the epoch of protogalaxy formation in an expanding universe are $Z = 10, 20$ and 60 for $q_0 = 2, 0.5$ and 0.02 , respectively, and do not apply to a universe which had a bounce in the past. Considering this and the order of magnitude nature of our own calculation, our implicit assumption that galaxies (or at least dusty protogalaxies) existed at $Z \approx 40$ is not unreasonable. Also, at $Z \approx 40$, the galaxies still occupy $\leq 1\%$ of the volume of the metagalaxy.

The number density of galaxies (or protogalaxies) at this epoch ($Z \approx 40$) $\geq 7 \times 10^4 N_{og}$, and this easily exceeds all lower limits for this number density of discrete sources set by the observed small-scale spatial isotropy of the microwave background radiation⁷.

Just as the radiation received from the Sun gives us direct information only about its surface, the microwave background radiation gives us direct information only about the 'surface of last scattering' when the radiation finally decoupled from matter and beyond which the metagalaxy remained transparent.

According to our model, this 'surface of last scattering' was the total dust distribution in galaxies or protogalaxies at the epoch $Z \approx 40$. Consequently, we cannot obtain direct information about the metagalaxy at earlier epochs ($Z > 40$), as it was then opaque. This conflicts with the detailed canonical model of the hot big bang cosmology which identifies this 'surface of last scattering' with a rapidly recombining plasma of temperature $T \approx 3,000 \text{ K}$ at a much later epoch $Z \gtrsim 1,000$, when the coupling mechanism between the matter and radiation was Thompson scattering (for example, see ref. 19).

Despite this conflict, however, we do not claim that the observed microwave background radiation is inconsistent either with the basic concept of a hot big bang cosmology, or with a completely different class of evolutionary cosmology, for example, the symmetric cosmology of Klein²⁰⁻²², where the minimum radius of the metagalaxy was $> 0.01 R_0$.

We stress that the observed cosmic microwave background radiation does not give us direct information about the state of the metagalaxy further back than the epoch corresponding to $Z \approx 40$, when galaxies or protogalaxies already existed, and when its own temperature was only about 110 K . To claim that it is strong evidence in support of the hot big bang cosmology whose earliest epochs correspond to $Z \gtrsim 10^{12}$ with corresponding temperatures of matter and radiation $> 10^{10} \text{ K}$, is completely unjustified.

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Radiative acceleration of gas above a luminous disk

Spherically symmetric radiative acceleration has been considered¹ as a mechanism for the ejection of matter from quasi-stellar objects. I present some calculations showing that in a simplified case, a strongly beamed outflow will result if the source of the driving radiation is not point-like but a disk.

Consider an infinitesimally thin, optically thick disk that emits thermal radiation with an intensity $I(r)$. The radiative force exerted by a surface element $r \, dr \, d\phi$, situated at cylindrical coordinates $(r, \phi, 0)$, on a spherical cloud with cross section S is

$$dF = (S/c) [2 \, hr \, I(r) (h^2 + R^2 + r^2 - 2rR \cos \phi)^{-3/2}] \times (h^2 + (R - r \cos \phi)^2)^{-1} (h, R - r \cos \phi) \, dr \, d\phi \quad (1)$$

where $(R, 0, h)$ are the cylindrical coordinates of the cloud. If the distance $D = (h^2 + R^2)^{1/2}$ of the cloud from the disk centre is large compared with the effective disk radius, one finds by direct integration of equation (1)

$$F \approx \frac{SL}{2\pi c} \frac{h}{D^3} \mathbf{e} \quad (2)$$

where L is the total luminosity of the disk and $\mathbf{e}$ is a unit vector pointing radially away from the disk centre. The net force on a cloud with mass m is due to the sum of F and the gravitational attraction of the disk and its central object. If the latter is dominant and has mass M , the net force is

$$F = \frac{\mathbf{e}}{D^2} \left(\frac{SL}{2\pi c} \frac{h}{D} - MGm \right) \quad (3)$$

Apparently, this force is directed away from the central object if

$$h \gtrsim R(4\epsilon^2 - 1)^{-1/2}, \quad \epsilon \equiv SL/(4\pi mc MG) \quad (4)$$

where ϵ is the Eddington number. Equation (4) defines a cone above the disk, the opening angle of which becomes larger with

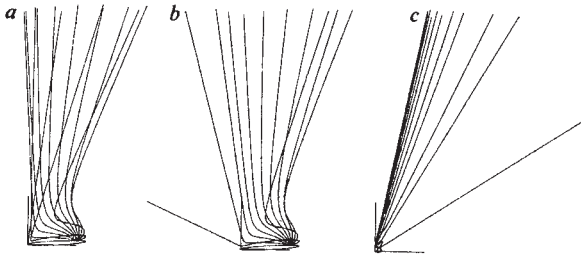


Fig. 1 Orbits of clouds in the force field given by equation (3), with Eddington number $\epsilon=1$. Solutions were made dimensionless by scaling with length unit r_0 (horizontal and vertical lines) and time unit $(MGr_0^{-3})^{-1/2}$. Plot marks indicate time intervals of 0.5. *a*, All initial velocities in the plane of the drawing. Initial velocity modulus 0.5, stepped by 15° from -90° to $+90^\circ$. *b*, Initial velocities as in (*a*), but all with initial velocity 0.1 added tangential to the disk. *c*, Same rotated through 90° . Every cloud passing through the disk is probably stopped there, which makes the beam narrower than shown here.

increasing luminosity L . The existence of this cone is the cause of the beamed outflow. Equation (4) has solutions if

$$\frac{2\pi m}{S} < \frac{L}{MGc} = 9.62 \times 10^{-3} \left(\frac{LM_\odot}{L_\odot M} \right) \text{ kg m}^{-2} \quad (5)$$

The cloud must be optically thick, so that $m/S > m_H/\sigma$ where σ is a scattering cross section. If σ equals the Thomson cross section, the 'cloud' is an individual particle, and equation (5) is the Eddington condition.

I have considered two types of motion in the far field (3), namely the motion of individual clouds or particles, and the motion of an atmosphere. The former is a straightforward problem of classical mechanics, which was solved numerically by a fourth order predictor-corrector method (Fig. 1). The motion of a stationary atmosphere was considered for a dust

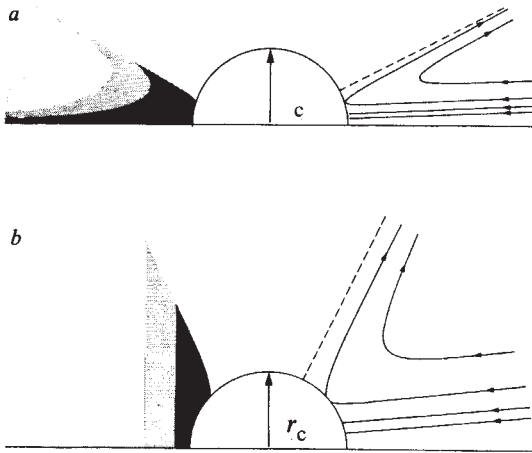


Fig. 2 Gas flow in the far field of the disk, if the gas pressure is negligible. The solutions have been made self-consistent by requiring that the accretion onto the central object with radius r_c generates exactly the luminosity corresponding to the Eddington number of the flow pattern. *b*, $A = -1$ [see equation (1)], $\mu = 0.01$; these parameters imply $\epsilon = 1.42$ and a disk thickness at infinity of $z = 4.74 r_c$. *a*, $A = -1.25$, $\mu = 0.01$, yielding $\epsilon = 3.43$ and $z = 0.98 r_c$. It has been assumed that σ equals the Thomson cross section, $\psi r_c^A = 10^{-2} \text{ kg m}^{-3}$, $r_c = 10^6 m$, $M = M_\odot$, and m equals the mass of the proton. It seems that for $0 < \mu < 1$, the self-consistent Eddington number is $1.35 < \epsilon < 3.57$ if $A = -1$, and $3.25 < \epsilon < 6.83$ if $A = -1.25$. Further exploration of equation (14) indicates that for reasonable γ , ϵ is typically rather less than 5.

model (negligible gas pressure). In spherical coordinates (r, φ, θ) the equations for this case are

$$uu_r + \frac{v}{r} u_\theta - \frac{v^2}{r} = -\frac{MG}{r^2} (2\epsilon \cos\theta - 1) \quad (6)$$

$$uv_r + \frac{v}{r} v_\theta + \frac{uv}{r} = 0 \quad (7)$$

$$\rho(u_r + 2\frac{u}{r} + \frac{1}{r} v_\theta + \frac{v}{r} \cot\theta) = -u\rho_r - \frac{v}{r} \rho_\theta \quad (8)$$

where $(u, 0, v)$ is the velocity vector and a subscript denotes partial derivation. The full equations, including azimuthal motion and a viscous dissipation term, also admit the type of similarity solutions that will be described below. These have been calculated also, but are omitted here for the sake of brevity; they are alike to the solutions given here, so that the main conclusions regarding the beaming and the influence of the Eddington number are not altered. Separating the variables by putting $v = f(\theta)$ $(MG/r)^{1/2}$ and $u = -2 (MG/r)^{1/2} \partial f(\theta)/\partial \theta$, one obtains the ordinary differential equation

$$2\left(\frac{df}{d\theta}\right)^2 + 2f\frac{d^2f}{d\theta^2} + f^2 = -2\epsilon \cos\theta + 1 \quad (9)$$

The streamlines follows from u and v as

$$\frac{u}{v} = \frac{1}{r} \frac{dr}{d\theta} = -2 \frac{d \log f}{d\theta} \rightarrow r \propto f^{-2} \quad (10)$$

The density is found from equation (8) to be

$$\rho = \psi r^A f(\theta)^{2A+2} / \sin\theta \quad (11)$$

Further solutions for ρ can be generated from equation (11) by putting $\psi = \psi(A)$, solving A from $(\partial\rho/\partial A) = 0$, and substituting the solution into (11). Equation (9) has the solution

$$f = \{1 - 2\epsilon[\alpha \cos\theta + (\beta + \frac{1}{2}\theta) \sin\theta]\}^{1/2} \quad (12)$$

The boundary conditions at $\theta = \pi/2$, $r = \infty$, dictate $\beta = 1/(2\epsilon) - \pi/4$ and $\alpha = \frac{1}{2} - \mu/\epsilon$, where μ is a small number determining the thickness $z = r_c f^2(\theta_c)/2\mu$ of the disk at infinity. Here θ_c is the angle at which the flow is just tangential to the central object with radius r_c (Fig. 2). The boundary conditions at $r = r_c$ determine the value of ϵ implicitly, as follows. Integration of ρu over the region $\theta_c < \theta < \pi/2$ gives the accretion rate

$$\dot{M} = 4\pi\psi r_c^{A+2} f_c^{2A+3} (MG/r_c)^{1/2} (2A+3) \quad (13)$$

where $f_c = f(\theta_c)$. Because $L \approx 3M\dot{M}G/r_c$, it follows from equation (4) that

$$\gamma\epsilon = f_c^{2A+3}, \gamma \equiv \frac{mc}{S} \frac{2A+3}{3\psi r_c^A} (MGr_c)^{-1/2} \quad (14)$$

Now θ_c is the solution of $(\partial f/\partial \theta)(\theta_c) = 0$; because $f = f(\epsilon, \mu)$ one has $\theta_c = \theta_c(\epsilon, \mu)$, whence equation (14) becomes an implicit equation for ϵ with solution $\epsilon(\mu)$. For given boundary conditions at $r = \infty$, there is only one ϵ that makes the flow fit at $r = r_c$ (Fig. 2).

To obtain the force field near the disk, equation (1) must be integrated numerically. This precludes simple analytic hydrodynamics, so I have only numerically integrated the equations of motion for individual clouds or particles in the near field (Fig. 3).

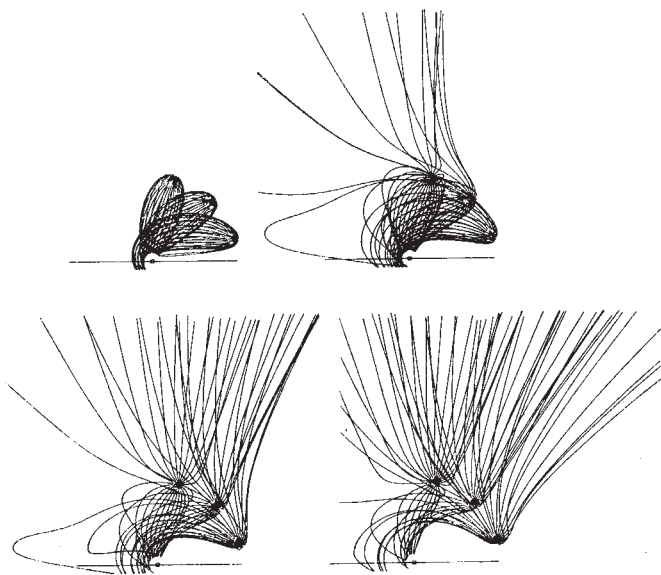


Fig. 3 Orbits of particles in the near force field of equation (1). The particles were radiated isotropically in the plane of the drawing with initial velocity 0.25 (normalisation as in Fig. 1), starting one disk radius away from the central object. Eddington numbers are 2, 3, 4, and 5, respectively. Note that even near the disk, beaming is rapidly established. The % of particles blown away is, respectively: 0, 18, 47, 70. These high values suggest a self-regulatory mechanism for the disk luminosity, by non-acceptance of infalling material when $\varepsilon \gtrsim 2.5$. Since strong beaming occurs for low ε only, this regulation indirectly helps to maintain the collimated outflow.

Apparently it is possible to establish strong beaming within a distance of the order of the disk radius. Thus X-ray sources with double radio structure^{2,3} and extragalactic radio doubles could in principle derive their shape from an asymmetry of their central radiation field. A proper treatment of this asymmetric acceleration; however, will have to deal with radiative transfer¹ and must include considerations about the spectrum of the disk radiation, Rayleigh-Taylor instability of the accelerated material (which perhaps gives rise to clouds in the first place), and possibly the influence of magnetic fields. The problems involved are too extensive to be readily estimated, but probably the beaming will persist even when some radiation scattering is present. The reason to expect this is that, to first order, the radiation removed from the anisotropic component of F by scattering through an optical thickness τ will emerge as isotropic radiation pressure, which counteracts the influence of gravity:

$$Fr^2/MG \approx 2\varepsilon e^{-\tau} \cos \theta + \varepsilon(1 - e^{-\tau}) - 1 \quad (15)$$

Near $\varepsilon = 1$, the value of θ where $F = 0$ (that is, the opening angle of the cone within which the force is directed outward) does not depend strongly on τ ; for example if $\varepsilon = 1.5$, the opening angle increases from 70° at $\tau = 0$ to 90° at $\tau = 1.1$.

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Magnetic field amplification in interstellar collisionless shock waves

It is commonly assumed that a simple compression of the magnetic field occurs in interstellar shock waves. Recent space observations of the Earth's bow shock show that turbulent amplification of the magnetic field can occur in a collisionless shock. I show here that radio observations of Tycho's supernova remnant indicate the presence of a shock wave with such magnetic field amplification.

A collisionless shock wave can be characterised by three parameters: the Mach number, M , or the Alfvén Mach number, M_A ; the preshock ratio of thermal to magnetic pressure, β ; and the angle between the flow direction and the magnetic field, θ (compare with ref. 1). Formisano and Hedgecock² classified the structures of the Earth's bow shock as a function of these parameters. They found that in shocks with $M_A > 3$, the degree of turbulence increased with β . The dividing line between laminar and turbulent flow occurred at $\beta \sim 0.1$. A series of observations of high β bow shock structures have been reported by Formisano *et al.*³, who found magnetic field increases in the shocks which were much larger than normal. Typical field increases are by a factor of 2-4, but here increases by a factor of 20 or more were noted. In fact, in the first shock ($\beta = 8.0$, $M = 6.5$), the energy density in the postshock field was about equal to the dynamic pressure of the upstream solar wind; in the second ($\beta = 170$, $M = 7.4$), it was $\sim 15\%$ of the wind pressure, and in the third ($\beta = 49$, $M = 7.3$), it was $\sim 30\%$ of the wind pressure. There is at present no theory for the macroinstabilities which give rise to the turbulent amplification of the magnetic field.

Despite the lack of theoretical understanding, the possibility of field amplification in interstellar shock waves should be considered. In Tycho's supernova remnant, there is evidence for the presence of a collisionless shock. M and β of a shock are

$$M = 7.1 (V_s/100 \text{ km s}^{-1}) (T/10^4 \text{ K})^{1/2}$$

$$\beta = 3.9 (T/10^4 \text{ K}) (n/1 \text{ cm}^{-3}) (B/3 \times 10^{-6} \text{ G})^{-2}$$

where V_s is the shock velocity and T , n , and B refer to the temperature, density, and magnetic field of the ambient medium which is assumed to be ionised. M_A is proportional to $M\beta^{1/2}$. The distance to Tycho's remnant is uncertain; distance dependent quantities will be given in terms of D_6 , which is in units of 6 kpc (refs 4, 5). Motions of the optical filaments in Tycho's remnant imply a velocity of $6200 D_6 \text{ km s}^{-1}$ (ref. 6). The filaments appear along the outer edge of the radio emission (J. R. Dickel, personal communication), so they probably outline the shock front. In many places, the outer edge of the radio emission is unresolved at 6 arc s resolution⁷, again providing evidence that this defines the shock front. The Coulomb mean free path of the hot postshock gas is a significant fraction of the radius of the remnant, indicating that collisionless heating of the gas occurs. The Mach number is larger than 100, which is greater than the Mach number of observed shock waves in the Solar System. There is no reason to expect a collisionless shock to become less turbulent with increasing M .

The height of Tycho's remnant above the galactic plane is $160 D_6 \text{ pc}$. The density and magnetic field are not well known at this altitude, but it is likely that $\beta > 1$. X-ray observations of the remnant indicate a high ambient density, $n \sim 4 \text{ cm}^{-3}$ (ref. 8). Stability of the gas to the Rayleigh-Taylor instability in the galactic gravitational field may also require $\beta > 1$. Thus, on the basis of observations of the Earth's bow shock, it is expected that turbulent magnetic field amplification occurs in the shock wave of Tycho's remnant.

This hypothesis is supported by the radio observations of the remnant. Van den Bergh⁶ found evidence from the filament motions that the remnant is in the adiabatic blast wave phase of evolution. The postshock flow can be described by a similarity

solution. Duin and Strom⁷ found that the observed radio polarisation, which implies a radial orientation of the magnetic field, could be quantitatively accounted for by the similarity solution because of the radial stretching in the postshock flow. This model is, however, viable only if the magnetic field is randomised in the shock wave. If only tangential compression occurred in the shock, a very particular magnetic field alignment would be necessary to give the observed polarisation direction. Because a radial field is implied by observations of several young remnants, this is unlikely. Thus, we have evidence that the magnetic field has been randomised in a turbulent collisionless shock.

Next, we consider to what extent the magnetic field is amplified in the shock wave on the basis of the nonthermal radio flux. First assume that there is no turbulent field amplification. The postshock magnetic field is probably less than 1.2×10^{-5} G because the ambient field is likely to be smaller than 3×10^{-6} G. If this field occupies 25% of the supernova remnant volume, the magnetic energy is $5 \times 10^{46} D_6^3$ erg. In order to produce the observed nonthermal radio radiation, a relativistic electron energy of $2 \times 10^{49} D_6^2$ erg is required. This is an extreme lower limit to the relativistic particle energy because it assumes that the magnetic field 160 D_6 pc from the galactic plane is the same as that in the plane, that the maximum field compression occurs in the shock, and that there is negligible energy in relativistic protons; the implied energy may actually be an order of magnitude higher. As the total energy release in the supernova is probably less than 10^{51} erg, this is a large fraction of the supernova energy. It is unlikely that such a high acceleration efficiency can be achieved, especially because adiabatic deceleration would be the main process acting on the particles in the absence of turbulence. On the assumption that there is no energy in relativistic protons, the equipartition field in Tycho's remnant is $6 \times 10^{-5} D_6^{-2/7}$ G, which would be accompanied by a particle energy of $2 \times 10^{48} D_6^{17/7}$ erg. The corresponding magnetic field pressure is only $0.02 n^{-1} D_6^{-18/7}$ % of the dynamic shock wave pressure. The required increase in the magnetic field, a factor of about 20, is comparable to that observed in high- β bow shocks. It is likely that the magnetic field has been turbulently amplified in the collisionless shock wave.

The turbulent hydromagnetic motions may result in stochastic particle acceleration. Energetic particles are frequently observed in association with collisionless shocks in the Solar System. This subject is important in considering the radio emission from supernova remnants in the adiabatic phase of their evolution. The possible presence of turbulent collisionless shocks should also be considered in models of active galactic nuclei and double lobe radio sources.

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Lack of dust in quasar absorption line systems

THE origin of the absorption line systems in quasars is still uncertain¹. Most such systems apparently have column densities of atomic hydrogen of the order of 10^{19} cm⁻², but, at least two quasars, 1331+170 (ref. 2) and PHL 957 (ref. 3), have such strong Lyman α absorption lines that atomic hydrogen column densities of the order of 10^{21} cm⁻² are indicated. It should be possible to observe the dust produced 2,200 Å extinction bump as it is redshifted into the visible⁴, and to determine whether the

absorption line systems are produced in spiral galaxies where the dust content is similar to that in the interstellar medium. McKee and Petrosian⁴ argue that the emission line regions of quasars generally lack dust, and that toward PHL 957 the 2,200 Å feature is absent. From recent published data, I argue that dust similar to that found in the interstellar medium is not found toward the quasars 1331+170 and PHL 957. This could explain why H₂ is not found toward PHL 957, and it also indicates that the absorption line systems in quasars are not produced in spiral galaxies similar to ours.

Carswell *et al.*² measured the profile of the Lyman α absorption line toward 1331+170, from which they estimated that the line centre is redshifted to 3,370 Å. From their Fig. 3a, it seems that although the data are noisy, the residual intensity of the line profile reaches a value of 0.5 at about 3,335 and 3,415 Å to the blue and red, respectively. It therefore seems that the Lyman α line centre is at 3,375 Å, which agrees with redshift system A at $z = 1.7755$ (refs 2, 5). There is also a redshift system at $z = 1.7852$, but in general the equivalent widths in system B are smaller than the equivalent widths in system A (ref. 2). It is likely that most of the hydrogen toward 1331+170 is in system A. In any case, the Lyman α line is so wide that it probably lies on the damping portion of the curve of growth, and the precise line centre does not affect the estimate of the atomic hydrogen column density, $N(\text{H})$. (Observations with higher signal-to-noise should be obtained to be certain that the Lyman α profile can be represented by damping wings). The Lyman α half width at half maximum (HWHM) is 40 Å. In the rest frame of the absorption line system, the HWHM is 14 Å, and $N(\text{H})$ equals 3×10^{21} cm⁻² (ref. 6).

In our Galaxy, the dust-to-gas ratio is generally uniform to within a factor of two (ref. 7). We adopt $E(B-V)/N(\text{H}) = 0.2 \times 10^{-21}$ mag cm⁻² (refs 8, 9). Assuming a ratio of total to selective extinction of $R = 3.3$ (ref. 10) and taking the standard extinction curve for the 2,200 Å bump of Bless and Savage¹¹, then for representative wavelengths the dust optical depth may be written as $\tau(2,500) = 6.8 E(B-V)$, $\tau(2,170) = 9.3 E(B-V)$ and $\tau(2,000) = 8.2 E(B-V)$. In all stars with sufficiently great reddening for the extinction to be measured accurately, this bump is present with a strength within a factor of two of its average values¹².

If $N(\text{H}) = 3 \times 10^{21}$ cm⁻² toward 1331+170 and if the dust-to-gas ratio in the absorption line system is similar to that in the interstellar medium, we would expect that $E(B-V) = 0.6$, and would expect to observe dust optical depths at 6,940, 6,020 and 5,550 Å of 4.1, 5.6 and 4.9, respectively. If lines are ignored, the flux density between 5,550 and 6,940 Å is observed to be constant to within a factor of 1.2 (ref. 5). If the dust-to-gas ratio were normal and assuming a flat spectrum, we would expect flux densities at 6,020, 5,550 and 6,940 Å to be in the ratios 1:2:4. Although a more precise analysis is possible, it seems that the dust-to-gas ratio toward 1331+170 is at least a factor of 20 less than in the interstellar medium.

From the measured equivalent widths² of the Fe II and Si II lines in the $z = 1.7755$ system, we find that even if these lines lie on the linear portion of the curve of growth, these species have column densities on the order of 3×10^{14} cm⁻². Therefore the gas phase abundances of the refractory elements iron and silicon toward 1331+170 is comparable to the gas phase abundances of the same species toward ζ Oph (ref. 13). There is no reason to suppose that the lack of dust toward 1331+170 results from a lack of metals.

The column density of atomic hydrogen toward PHL 957 is $7.5 \pm 2.5 \times 10^{20}$ cm⁻² (ref. 14). Except for a very broad C III line, between 6,000 and 9,000 Å the flux density seems to be a power law within a factor of 1.2 (ref. 14). In the absorption line system at $z = 2.3088$, we would expect a flux density variation between 7,180 and 8,270 Å (corresponding to 2,170 and 2,500 Å in the rest frame) of a factor of about 1.5. It therefore seems that there is a lack of normal dust toward PHL 957 by at least a factor of two, in rough agreement with McKee and Petrosian's estimate⁴.

I conclude that the absorption line region toward 1331+170 and probably the region toward PHL 957 are lacking dust similar to that in our own Galaxy. This can explain the lack of H_2 in these systems^{14,15}. The column density of atomic hydrogen toward 1331+170 is so high, however, that it is unlikely that we are observing this quasar through a galactic halo¹⁶ where the dust content might be unusually low. In the disk of a spiral galaxy, we would expect the dust/gas ratio to be comparable to the value in the interstellar medium, and it seems unlikely that the absorption line system at $z = 1.7755$ toward 1331+170 is produced in a spiral galaxy similar to ours.

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Relationship between atmospheric electricity and microwave radio propagation

ABRUPT changes in received polarisation coincident with lightning strokes have been seen on a 20 GHz satellite-to-earth radio link. These effects, and the surprisingly high levels of atmospheric cross polarisation observed on satellite links, have been tentatively attributed to high altitude ice crystals and their possible alignment by electric fields^{1,2}. In this paper we shall add to the existing data by presenting a precise measurement of the time scale of the abrupt polarisation changes and an event showing a striking correlation between the electric potential gradient at the ground and the cross-polarisation of signals received from the satellite. This is believed to be the first time that direct measurements of atmospheric electric fields have been related to microwave propagation measurements.

The linearly polarised 20 GHz beacon signal from the NASA ATS-6 geostationary satellite was received at the Bradford University, Oxenhope Laboratory during the period October 1975 to July 1976, while the satellite was stationed at longitude 35°E. At the receiving site (which is 450 m above sea level) the satellite was visible at 20° elevation with a 23° polarisation counter-clockwise from the vertical. Both the 'copolarised' and the orthogonal (or 'cross-polarised') received signals were measured. Without atmospheric hydrometeors present on the radio path, the cross-polarised component was typically >35 dB below the co-polarised component. A co-sited range-gated radar provided a quantitative measurement of reflectivity along the satellite radio path¹.

It is now apparent that the cross-polarisation measured on a microwave or millimetre wave satellite radio path can be an order of magnitude greater than that experienced on a terrestrial link for the same attenuation¹⁻³. The cross polarisation measured on a terrestrial path agrees with that predicted from a rainfall model assuming anisotropy to arise from non-spherical raindrops^{3,4}, whereas small, high altitude ice particles (possibly needles or plates) can cause

significant cross-polarisation on a satellite path^{1,3,5,6}. This high-cross polarisation, not related to attenuation, as observed on satellite radio paths has been termed 'anomalous' although this description may be questioned.

During 1,050 h of measurements with ATS-6 (in discrete sessions of typically 4 h per d) nine separate 'anomalous' events were recorded (that is, events involving separate weather structures). Typically, as a rainstorm moved over the receiving site, high (anomalous) cross-polarisation, varying on a time scale of minutes, was observed at such times when the slant radio path intercepted the frozen particles in the storm structure¹. In addition, during a thunderstorm on 7 May, 1976, abrupt changes in cross polarisation were observed (Fig. 1), in which the cross-polarised signal increased suddenly by several dB relative to the copolar level, and then returned close to the value before discharge in ~45 s. Of the twenty abrupt changes recorded during this event, four coincided with lightning strokes, as noted by observers on site for a short period of the storm. The other abrupt changes in cross-polarisation may also have been associated with lightning.

The rise times of the 15 largest abrupt cross-polarisation changes were found to be between 0.1 and 0.25 s, from FM tape recordings taken in a 500 Hz bandwidth. Sixteen

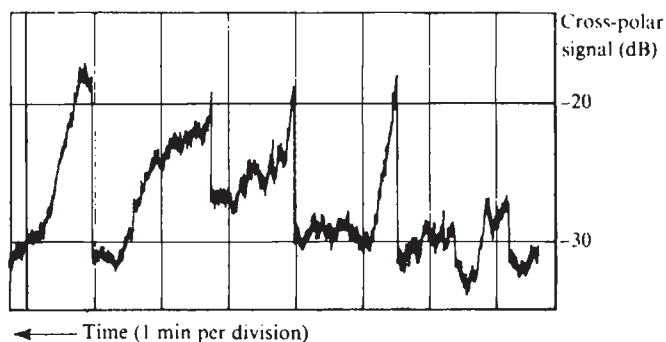


Fig. 1 Abrupt changes in cross-polarisation during a thunderstorm.

of the abrupt changes showed a rapid rise in cross-polarisation, whereas the remaining four were decreases. These changes are self evidently not 'sferics' (in view of the relatively long decay times) and were only seen in the one event during ATS-6 sessions which showed pronounced lightning activity. Identical changes were observed with two independent, coherent receivers for the cross-polarised signals and furthermore, no abrupt changes were seen in the co-polarised signal.

Following the observation of changes in cross-polarisation coincident with lightning strokes, a point-discharge electric field probe⁷ and a photoelectric lightning detector were installed on site. The fine wire electrode of the field probe was 4 m above ground. Although no further lightning activity was recorded during satellite sessions, a strong correlation between anomalous cross-polarisation and point-discharge current was observed in three subsequent events, one of which, with a predominantly positive discharge current, is shown in Fig. 2. It is interesting to note that there is a better correlation between the probe current and cross-polarisation than between the co- and cross-polarised signals. In the other two events, a pronounced correlation between electric field on site and satellite path cross polarisation has been seen to occur with a time displacement.

To summarise, we have observed a pronounced correlation between electric field strength (measured near the ground) and cross-polarisation on a satellite radio path. Radar returns from high altitude (>3 km) particles, coincident with the appearance of high cross-polarisation, point

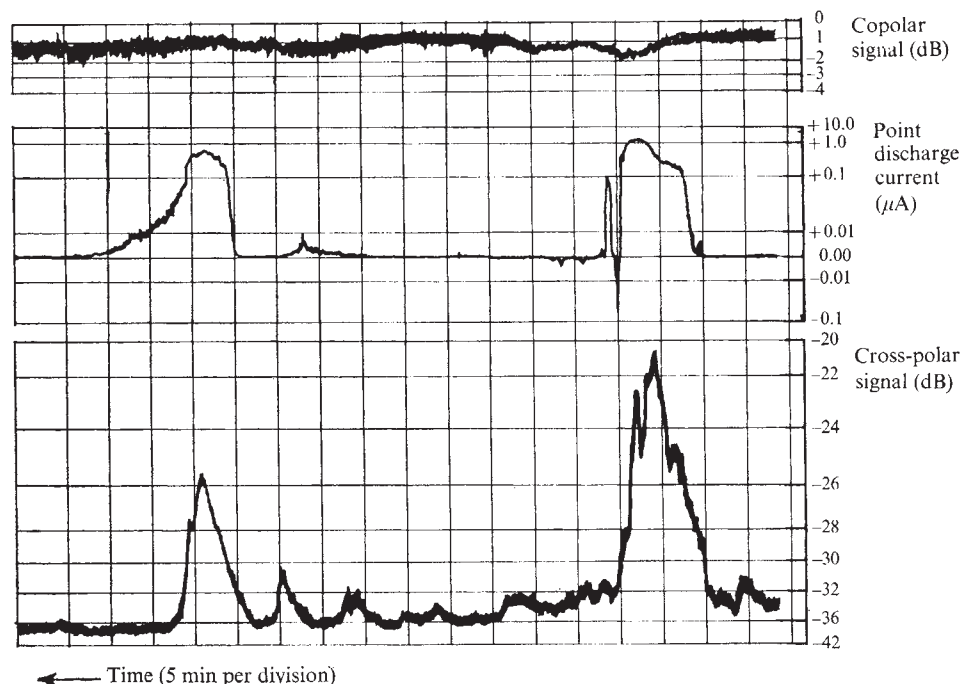


Fig. 2 Anomalous cross-polarisation and point-discharge current. Using an expression by Chalmers⁷ the electric potential gradient, derived from the point-discharge current, is estimated at a maximum of 5 kV m^{-1} for the first peak and 1.7 kV m^{-1} for the second peak.

to ice particles as the cause for such cross-polarisation^{1,2}. Analysis of the scattering from spheroidal ice particles^{5,6} shows that high cross-polarisation can occur with small particles for low signal attenuation, provided that some degree of particle orientation is present.

Hendry and McCormick⁸ have recently reported a high degree of orientation of ice particles from dual circularly polarised radar observations, which they have explained in terms of particle alignment in an electric field. 10^5 V m^{-1} has been shown to provide sufficient torque for rapid ($\sim 0.1 \text{ s}$) orientation of small ice spheroids⁸.

We also interpret our results in terms of the orientation of small ice particles (1 mm or less) in the electric fields associated with convective storms. We emphasise that a degree of particle orientation does not necessarily imply a high degree of instantaneous alignment. Without significant damping forces imposition of an electric field on a randomly orientated group of ice needles or plates will produce simple harmonic motion around a preferred (average) orientation. The depolarisation from ice needles or plates⁶ is such that only a small degree of preferred orientation is necessary for cross-polarisation.

In certain regions of storms aerodynamic turbulence will tend to disrupt field alignment, however it seems that in the upper regions of storm structures (typically $>5 \text{ km}$ in summer) turbulence is sufficiently low to permit a high degree of orientation⁸. Also the rapidity of alignment for small particles in strong fields, should permit realignment in the presence of turbulence provided that the latter is not overwhelming.

Alignment under aerodynamic forces alone is conceivable, but this does not explain the rapid lightning-correlated rises in cross-polarisation or the correlation between electric field and cross-polarisation.

The abrupt increases in cross-polarisation that we have observed may be interpreted in terms of the redistribution of charge in a thunderstorm at the incidence of a lightning stroke, resulting in a change in particle orientation. We emphasise that for linear polarisation a change in particle orientation with respect to the polarisation plane of the incident wave could result in either an increase or decrease in cross-polarisation, but a measurement with circular polarisation would show cross-polarisation related directly to the degree of particle orientation. Since coherent receivers were used for extraction of our cross-polarised

signals (phase locked to the copolar signal), explanation of the abrupt cross-polarisation changes in terms of incoherent emissions from ionisation or lightning flashes is not credible.

If the rapid, lightning-correlated cross-polarisation changes that we have observed are caused by particle re-orientation then we must conclude, from the observed orientation times, that small particles are responsible. Small particles are also inferred from the absence of significant attenuation during anomalous cross-polarisation^{5,6}.

The precise nature of electric fields in thunderstorms is a matter of current debate⁹ and we hesitate to be dogmatic about the model applicable to our observations. Measurements of satellite cross-polarisation with circular polarisation would help clarify this issue. Apart from the implications of our results for the communications engineer, we would expect our results to be of relevance to the understanding of thunderstorm models.

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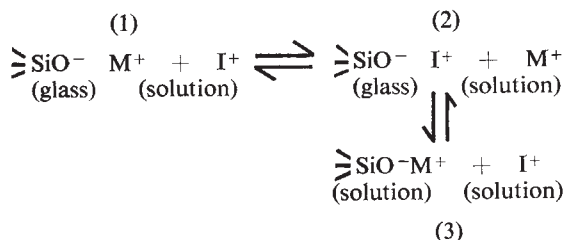
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Decomposition of silicate glasses in alkaline solutions

WHEN a silicate glass comes into contact with a neutral or a slightly alkaline aqueous solution the only reaction which occurs is a diffusion controlled hydrogen-alkali ion exchange. The silica network is stable. In solutions with $\text{pH} > \text{about } 9$, the network starts to break down at its interface with the solution. The rate of breakdown increases sharply with in-

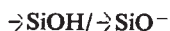
creasing pH; simultaneously the ion exchange rate decreases sharply. In solutions with $pH > \text{about } 12$ it is difficult to detect the alkali released in solution by classical microanalytical methods as the solution is primarily made up of alkali hydroxide. It has been repeatedly suggested that the ion exchange reaction ceases to occur under these conditions and that the decomposition process becomes only a network breakdown. Surface and in-depth concentrations of alkalis in a glass which has been subjected to a highly alkaline solution have been determined by Auger electron spectroscopy (AES). Our results indicate that the ion exchange does not cease to occur in highly alkaline solutions as commonly believed.

The decomposition may be represented by the following scheme:



where M denotes an alkali atom, usually sodium, while I denotes a solvated monovalent cation, usually a proton. This reaction scheme is widely used in discussing the physicochemical processes (corrosion, membrane potentials, electrokinetic phenomena, etc.) exhibited by glass and by many silicates.

The scheme often appears as two separate equations relating (1) $\rightleftharpoons$ (2) and (2) $\rightleftharpoons$ (3). Ion exchange processes which take place in aqueous solutions and involve a solvated proton as a reacting species are essentially acid-base reactions. Reactions (1) $\rightleftharpoons$ (2) and (2) $\rightleftharpoons$ (3) are related through the equilibrium constants of the conjugate



acid-base pair¹ by the relation $K_a K_b = K_w = 10^{-14}$ at 25 °C, K_a being of the order 10^{-10} , $K_b \sim 10^{-4}$.

In alkaline solutions where $a_{\text{M}^+} \gg a_{\text{OH}^-} \gg a_{\text{H}^+}$ a shift of the equilibrium towards positions (2) and (3) is favoured. The reverse occurs in acidic solutions. Studies on the kinetics of approach to the equilibrium of reaction (1) $\rightarrow$ (2) and (2) $\rightarrow$ (3) have been carried out in aqueous solutions buffered at pH values of 1–13. For pH of 1–9 the rate of dealkalisation remained constant, and independent of the pH of the solution, and sharply decreased with increasing pH thereafter. The rate of breakdown was extremely low in the pH range 1–9 and sharply increased with pH above the critical value of about 9 (ref. 1).

Chemical analysis of alkalis and silica in the glass and in solution, at various pH values, shows that the ratio $\text{M}_2\text{O}/\text{SiO}_2$ is always higher in acidic, neutral and slightly alkaline solutions than in the glass. This is considered¹ to imply that reaction (2) $\rightarrow$ (3) lags behind reaction (1) $\rightarrow$ (2) and a silica-rich leached layer is developed on the glass surface in contact with the solution. The existence of such a layer has been proved² by the establishment of in-depth composition profiles of glasses which have been in contact with aqueous solutions of varying pH.

As the pH of the solution increases above 9, the $\text{M}_2\text{O}/\text{SiO}_2$ ratio in the solution slightly decreases and tends to approach the same value as in the glass. Hence, it has been inferred^{3–6} that the decomposition of glass becomes entirely a dissolution process, that is, a network breakdown as represented by reaction (2) $\rightarrow$ (3). This inference is tempting, because it appears difficult for a solvated alkali ion in solution to re-enter the glass by reaction (2) $\rightarrow$ (1) to occupy a site originally filled by an anhydrous alkali ion. The almost linear rate of decomposition of glass in highly alkaline solutions has been considered to support such inference, but concrete evidence is lacking. Analytical solution chemistry is little value for deciding whether reaction (2) $\rightarrow$ (3) goes faster than reaction (2) $\rightarrow$ (1)

or continues to lag behind it because one would have to detect parts per million of the alkali species originally present in the glass in the presence of much higher concentration of the other alkali species which is used for buffering the medium. We have devised the following experiment to decide whether the breakdown of glass represented by reaction (2) $\rightarrow$ (3) supersedes the ion exchange reaction (2) $\rightarrow$ (1) under the extreme condition where $a_{\text{M}^+} > a_{\text{OH}^-} \gg a_{\text{H}^+}$. Two identical fresh rectangular samples were prepared by breaking down a commercial soda-lime-silica glass container which has not been subjected to any surface treatment. The approximate composition in weight per cent of the glass was as follows: 74% SiO_2 , 13% Na_2O , 12% ($\text{MgO} + \text{CaO}$) and 1% other oxides. The first sample was immersed in a solution of 0.1 M NaOH; the second in a solution of 0.1 M NaOH + 1.0 M Li_2CO_3 . Each sample was allowed to remain in contact with the solution for 5 h at 25 °C. Lithium was chosen as a tagging cation as the free energy change of its association with the $\rightarrow \text{SiO}^-$ sites makes it more favourable to other alkalis⁵. If reaction (2) $\rightarrow$ (3) proceeds faster than reaction (2) $\rightarrow$ (1), lithium could not be detected on the treated glass surface, and complete dissolution of the glass in highly alkaline solutions, already inferred by many workers, would become evident. If, on the other hand, Li^+ , not in association with carbon, from the CO_3^{2-} radical, with which it must be at least partly associated in solution, could be detected in the glass to

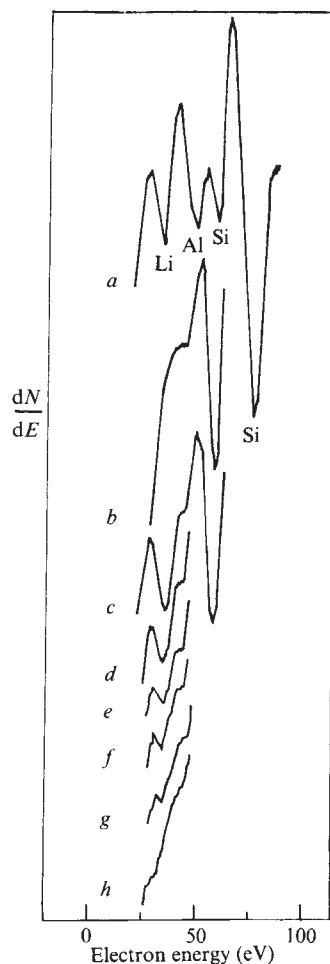
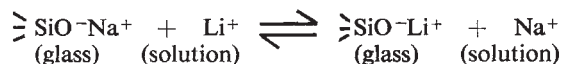


Fig. 1 Auger electron spectra for (a) Spodumene fracture surface (b) Soda-lime-silica glass surface treated in 0.1 NaOH (c) Soda-lime-silica glass treated in 0.1 N NaOH + 1.0 N Li_2CO_3 . (d–h) Sample c after bombardment with a 2.0 keV beam of argon ions for 0.5, 2.0, 6.0, 10.0 and 18.0 min, respectively. Beam voltage, 3 kV; beam current, 3 μA ($\sim 250 \mu\text{m}$ diameter); modulation amplitude, 5 eV; scan rate (0–100 eV), 2 eV s^{-1} ; time constant, 1 s; sensitivity, 1 μV .

some depth, this would indicate a decomposition process in which the ion exchange reaction still has a role.



AES was performed on the two glass samples treated in the manner outlined above. The technique used was that described by Pantano *et al.*² for glass surfaces. It involves cooling the samples to liquid nitrogen temperature, maintaining the beam current density at low value and minimising the electron irradiation time. Approximate surface and in-depth concentration of alkalis were determined from the spectra using an Ar ion-milling apparatus to remove surface material while simultaneously analysing with AES. The change in the Auger peak-to-peak height of each species is generally assumed to be proportional to the change in concentration of that constituent. Figure 1 shows the spectra obtained.

The spectra of a spodumene ($\text{Li}_2\text{O} \cdot \text{Al}_2\text{O}_3 \cdot 4\text{SiO}_2$) fracture surface was obtained as a standard, because of the difficulty of identifying the Auger transition for Li (Fig. 1a). The peak energy for the Auger transition assigned to Li is 37 eV, while the main Si peak appears at the 76 eV with a minor peak at 58 eV, and the Al peak appears at 51 eV. In Fig. 1b the only Auger transition in this energy range is due to Si (58 eV). The main silicon peak at 78 eV is not shown. In Fig. 1c in addition to Si, the peak identified as being due to an Li Auger transition is also detected. In Fig. 1d–h, the persistence of a Li signal for up to 10 min of ion milling ($\sim 250 \text{ \AA}$) suggests the existence of Li within the glass surface. Also, the sodium peak intensity of the surface treated with $\text{NaOH} + \text{Li}_2\text{CO}_3$ was approximately 40% less than that measured on the glass treated without Li. This is a reasonable result as the sites now occupied by Li would otherwise be occupied by Na. These results lead us to exclude complete dissolution, or glass network breakdown, as a possible mechanism for glass decomposition in these solutions and conclude that the ion exchange continues to have an important role even in highly alkaline solutions.

Ceramic materials and more than two thirds of the rocks constituting the Earth's crust are basically made of the same building unit as glass, that is, the silicon-oxygen tetrahedron, and consequently undergo the same sequence of reactions with aqueous solutions. The present conclusion possibly applies to other silica-based materials.

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A near perfect shape-memory ceramic material

AFTER high temperature plastic deformation and cooling under load to room temperature, glass-ceramics containing mica as the principal crystalline phase retain a near-perfect memory of their undeformed state, the plastic strain being recoverable by a subsequent high temperature anneal. Acti-

vation energy measurements support the hypothesis that dislocations in the mica crystals control the shape-memory process.

The elastic martensitic transformations responsible for shape-memory phenomena in certain metal alloys have been the subject of extensive research, recently reviewed by Wayman¹. In principle, any multi-phase system containing phases with different viscosities (but equal shear moduli) can also exhibit shape-memory behaviour since elastically strained components are capable of driving viscous elements back towards their original undeformed shapes. Such behaviour, by internally oxidised copper, has been demonstrated by Brown and Stobbs².

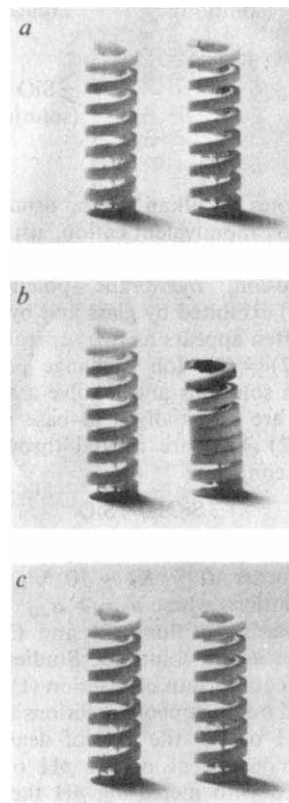


Fig. 1 The shape-memory behaviour of a mica glass-ceramic. The specimen on the right has been subjected to high temperature compression before unloading at room temperature (b) and then annealed at high temperature (c).

At temperatures $>300^\circ\text{C}$, mica can be deformed plastically by slip between its basal layers. Such deformation in crystals intimately mixed with a rigid, multiply connected phase should permit retention at room temperature of any small shape change imposed on the phase mixture at temperatures above 300°C ; since glide in mica is not possible at low temperature, removal of the mechanical constraint, after cooling to room temperature, is not accompanied by the reversal of plastic strains in the mica that would be required in order to release fully the elastic strain in the matrix. The elastic strain energy thus stored provides a driving force for recovering the undeformed shape, should the temperature subsequently approach 300°C . If the micaceous phase is singly connected, no plastic strain can leak to the free surface and, in principle, the phase mixture should be capable of returning precisely to its original shape.

The series of mica glass-ceramics developed at Corning Glass Works³ fit this specification for a perfect shape-memory solid. The volume fraction of fluorophlogopite, the

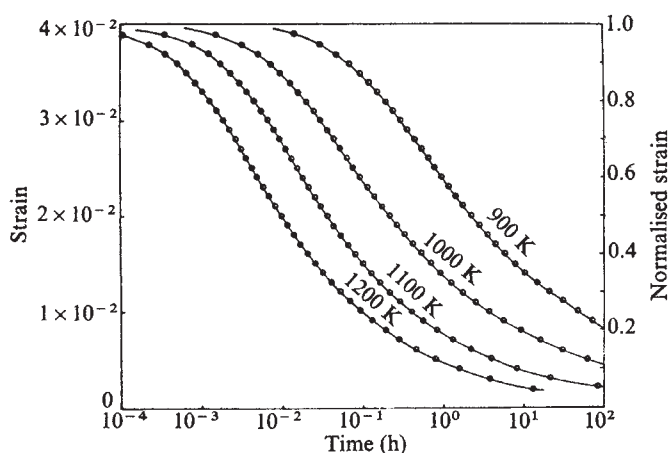


Fig. 2 Summary of torsional strain recovery data obtained from Corning 9650.

main crystalline phase, is typically 2/5 to 3/5, with maximum crystal diameters ranging from $\frac{1}{2}$ μm to 100 μm and aspect ratios of order 10:1. The mica glass-ceramics are easily machined using conventional tools, and helical specimens having outer diameter 2 cm and pitch 3.2 mm were cut from as-crystallised rods. Figure 1 shows two identical helical specimens machined from Corning code 9650, (a) before deformation, (b) after quickly cooling the specimen on the right from axial compression at 500 °C and (c) after subsequently annealing (b) for 2 h at 800 °C. Each individual pitch has recovered at least 87% of the imposed strain. In other preliminary experiments, recoveries of 99% after prolonged anneals have been attained.

Using improved specimens ultrasonically machined from Corning codes 9650 and 9658, accurate measurements of axial strain recovery have been made during annealing at several temperatures. The measurements have been converted to local torsional strain and Fig. 2 shows a summary

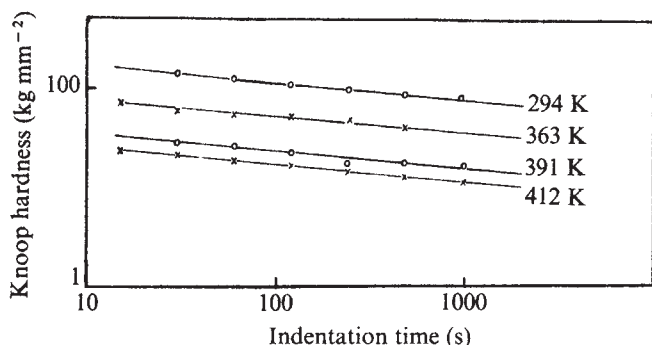


Fig. 3 Indentation creep of muscovite single crystals. (Long axis of Knoop indenter parallel to *a* axis.)

of the data for Corning code 9650. Similar data was obtained for glass-ceramic code 9658. For each material, the data from all temperatures may be superposed on to a master curve at, say, 1,000 °C merely by shifting the individual curves horizontally. Assuming that a single mechanism is rate controlling, the shift corresponds to an activation energy of 42 ± 5 kcal mol⁻¹ for Corning 9650, and 22 ± 3 kcal mol⁻¹ for Corning 9658. These are much lower than the activation energies for large scale, high temperature creep of the same mica glass-ceramics. In the temperature range

480–670 °C, for example, Corning 9650 tested in tension creeps with an activation of 100 kcal mol⁻¹ (James and Ashbee⁴). The larger activation energy is characteristic of flow of the glassy matrix, whereas the activation energy for shape-memory behaviour is expected to be that for dislocation glide in mica. A measurement for the latter, obtained from the temperature/time dependence of the microhardness of muscovite shown in Fig. 3, is 29 ± 4 kcal mol⁻¹.

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The use and misuse of pure water PVT properties for lake waters

ALTHOUGH dissolved substances affect the thermodynamic properties of lake waters,^{1,2} many limnologists still consider lake water as pure water^{3–8}. This can be a good assumption if used with caution: lake water is by no means pure water, especially when the precise pressure, volume, temperature (PVT) properties are considered. PVT properties of lake water can be determined from an equation of state for seawater provided that the total mass fraction of dissolved salts in seawater and lake water are equated⁹. In addition, the total mass fraction of dissolved salts affects calculations concerning the temperature of maximum density and thus stability¹⁰. Therefore, in the absence of direct PVT measurements on a particular lake, it is at present most appropriate to use an equation of state for seawater when examining effects of PVT properties in lakes. We present here a short equation of state determined with a precision of 2×10^{-6} g cm⁻³ in density over the appropriate range for most fresh water lakes, 0–0.6‰ salinity, 0–30 °C, and 0–180 bar. The equation of state is based on the 1 atm pure water density and compressibility equations of Kell¹¹, the pure water temperature and pressure effects of Fine and Millero¹², and the effects of dissolved salts of Millero *et al.*¹³ and Chen and Millero¹⁴:

$$d^P = d^0 / (1 - P/K) \quad (1)$$

$$d^0 \text{ (g cm}^{-3}\text{)} = 0.9998395 + 6.7914 \times 10^{-5}t - 9.0894 \times 10^{-6}t^2 + 1.0171 \times 10^{-7}t^3 - 1.2846 \times 10^{-9}t^4 + 1.1592 \times 10^{-11}t^5 - 5.0125 \times 10^{-14}t^6 + (8.221 \times 10^{-4} - 3.87 \times 10^{-6}t + 4.99 \times 10^{-8}t^2)S(\text{‰}) \quad (2)$$

$$K(\text{bar}) = 19652.17 + 148.376t - 2.329t^2 - 1.3963 \times 10^{-2}t^3 - 5.90 \times 10^{-5}t^4 + (3.2918 - 1.719 \times 10^{-3}t + 1.684 \times 10^{-4}t^2)P + (-0.8985 + 2.428 \times 10^{-2}t + 1.114 \times 10^{-2}P)S(\text{‰}) \quad (3)$$

where d^P and d^0 are the densities of lake water at applied pressures

P and 0 (sea level), respectively, t is the temperature in $^{\circ}\text{C}$, $S(\text{‰})$ is the salinity:

$$S(\text{‰}) = 0.9951437 g_T \quad (4)$$

where g_T is the total grams of dissolved salt in 1 kg of lake water¹⁵. The values of g_T usually increase with depth due to the increase of HCO_3^- , Ca^{2+} and nutrients¹⁶. The small changes in composition in a lake can be accounted for by making the appropriate changes in g_T . Further, Millero⁹ and Millero *et al.*¹⁷ showed that the densities calculated from the seawater equation of state for Lake Tanganyika water and artificial river water agree with the measured values to within $\pm 2 \times 10^{-6} \text{ g cm}^{-3}$ despite the large composition difference between the two waters. This verifies the validity of our equation of state for fresh waters.

One atmosphere densities computed from equation (1) at 0.15, 0.30, and 0.60‰ salinity over the temperature range of 0–30 $^{\circ}\text{C}$ are shown in Fig. 1. Also shown are the densities for pure water at 0 and 1.0 bar (gauge). It is clearly shown that even a nominal amount of salt, 0.15‰ salinity or 151 mg kg^{-1} , increases the density of pure water appreciably. At 0 $^{\circ}\text{C}$, the increase in density is $123 \times 10^{-6} \text{ g cm}^{-3}$, which is equivalent to a change of 2.4 bars in pressure or

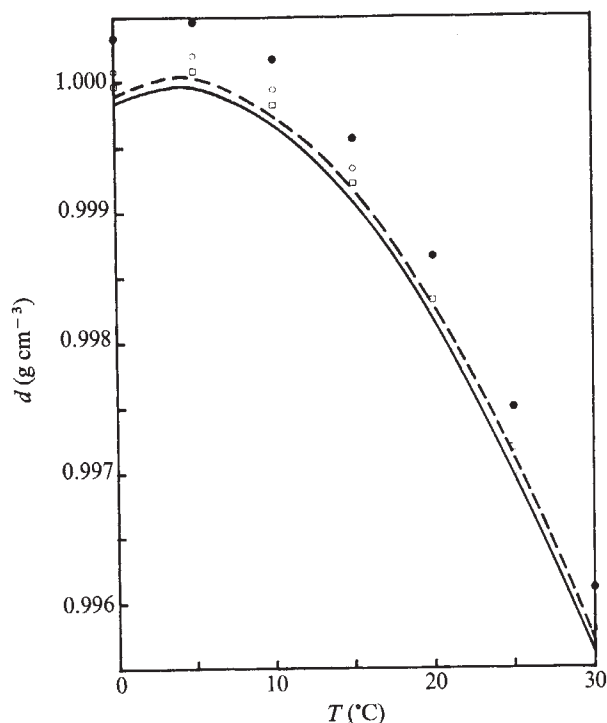


Fig. 1 Densities for pure water at 0 (—) and 1.0 (---) bar (gauge) and for lake waters at 0.15 (○), 0.30 (□) and 0.06 (△)‰ salinity at 0 bar (gauge) over 0–30 $^{\circ}\text{C}$.

2.9 $^{\circ}\text{C}$ in temperature. This increase in density has often been neglected and it is certainly not negligible.

The existence of a temperature of maximum density, T_{MD} , is of fundamental importance in limnology. An equation is given to be used to estimate T_{MD} with a precision of 0.001 $^{\circ}\text{C}$,

$$T_{\text{MD}} = 3.9839 - 1.9911 \times 10^{-2} P - 5.822 \times 10^{-6} P^2 - (0.2230 + 1.111 \times 10^{-4} P) S(\text{‰}) \quad (5)$$

At 1 atm, a nominal amount of salt, 150 mg kg^{-1} , in a freshwater lake contributes 0.033 $^{\circ}\text{C}$ to the depression of the temperature of maximum density. This seemingly small number, 0.033 $^{\circ}\text{C}$, which corresponds to the effect of 16.8 m of water, is orders of magnitude larger than the precision of the *in situ* temperature measurements and certainly should not be neglected. We, therefore conclude that the salt content is of significance in

freshwater lakes and our equation of state should be used to calculate reliable PVT properties for lake waters.

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Raman scattering and the characterisation of atmospheric aerosol particles

AIRBORNE particulates have a major role in the air pollution problem. They are responsible for acid rain, reduced visibility, and, in certain size ranges, are deposited in the lungs where they can cause various disorders. Considerable effort has been expended in the analysis of these particulates using techniques such as wet chemistry, X-ray fluorescence, infrared spectroscopy and ESCA. Yet there are still great uncertainties as to the chemical form and origin of many of the particulate species. We describe here preliminary studies of the feasibility of characterising particulate pollutants by means of Raman spectroscopy. We believe that this is the first attempt to apply this spectroscopic technique in this area of research. The samples studied included diesel exhaust particles, automobile exhaust particles (unleaded fuel, no catalytic converter) and several ambient air samples. The spectra from these samples were compared with those of polycrystalline graphite and activated carbon which were used as references. Our results indicate that physical structures similar to activated carbon are at least a major species and may be the dominant species in both source-enriched and ambient samples. The implications of this observation could be quite important in terms of atmospheric chemistry, health effects, weather modifications and the effects of aerosols on the albedo.

The beam from a Coherent Radiation argon ion laser (operating with 1 W at 5145 Å) was focused by a 75-mm focal length cylindrical lens to a spot of $0.06 \times 2 \text{ mm}$ on the sample surface, and the backscattered radiation was collected and imaged by an $f/3.4$ lens on to the slit of a Jarrell Ashe double monochromator. The incident polarisation of the laser was perpendicular to the slit of the spectrometer, and the scattered polarisation was not analysed. The output of the spectrometer was detected by an FW130 photomultiplier cooled to -20°C and used in a photon-counting mode. The photon pulses, after appropriate pulse shaping, were counted and displayed on a multichannel analyser. To minimise heating effects, the highly absorbing samples used in these experiments were rotated at 1800 r.p.m. by a motor—this increases the area illuminated by the laser beam by a large factor with almost no loss in signal level. The focal spot of the laser was located approximately 5 mm below the axis of rotation so that the effective illuminated area was an annulus of radius 5 mm and width 2 mm which yielded a rather low power density of $\sim 1.5 \text{ W cm}^{-2}$.

The samples used in these experiments were EDM 3 grade polycrystalline graphite (POCO Graphite Inc.), Norit A activated carbon (Pfanstiehl Labs), diesel exhaust collected on a glass fibre filter, automobile exhaust collected on a glass fibre filter from a number of cold starts of a poorly tuned 1974 Ford Pinto (lead-free fuel; no catalytic converter), and an ambient sample collected in 1975 as part of EPA's RAPS programme in St. Louis, Missouri. The latter sample was collected on a 1.2- μm Millipore filter using a dichotomous sampler¹ and was in the small size range fraction. The diesel and car exhaust samples were removed from the filter and transferred to an aluminium flat. This technique allowed us to obtain excellent Raman spectra of the particulates without interference from the large fluorescence of the filter material. This technique could not be applied to the ambient samples because of insufficient loading, and therefore in this case the Raman spectrum was obtained directly from the particles on the Millipore filter substrate.

Figure 1 shows the Raman spectrum obtained from automobile exhaust. Similar spectra were observed for diesel exhaust, activated carbon, and polycrystalline graphite with the dominant features of the spectrum occurring at 1,200–1,700 cm^{-1} . For polycrystalline graphite a strong line is also observed at $\sim 2,700 \text{ cm}^{-1}$ which we associate with a C–H vibration. In the ambient sample, where the signal to noise is severely limited by the large fluorescence background, the only lines that were clearly seen above the noise level were also in the 1,200–1,700 cm^{-1} spectral region. Figure 2 shows the Raman spectrum for the various samples in this region.

Koenig *et al.*² measured the Raman spectrum of a single crystal of graphite as well as that of polycrystalline graphite and activated carbon. In a single crystal only the Raman mode near 1,600 cm^{-1} is observed, and from a group theoretical analysis, it has been assigned to the $k=0 E_{2g}$ phonons of the graphite lattice. The mode near 1,350 cm^{-1} appears only in samples which are not perfectly ordered, and its intensity relative to the one near 1,600 cm^{-1} varies inversely with the crystallite size, L_a , as obtained from X-ray data. Solin *et al.*³ have shown that this ratio tends to saturate for crystallite sizes less than 40 Å. The identification of the 1,350 cm^{-1} mode is uncertain, but Koenig *et al.* suggest that

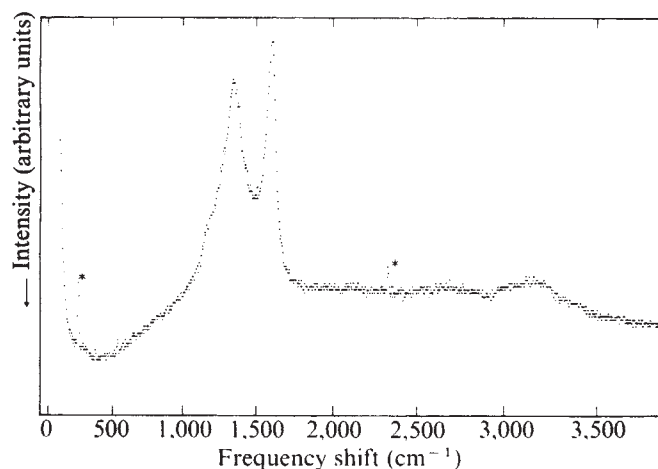


Fig. 1 Raman spectrum of automobile exhaust in the spectral region between 90 and 3,830 cm^{-1} . The slit width for this scan was 3 Å. The lines identified with an asterisk are due to grating ghosts.

it may be due to an A_{1g} phonon which is normally Raman inactive but is active in this case due to a breakdown of the k selection rules by the small crystallites in the sample.

It is evident from Fig. 2 that the spectra of activated carbon, diesel exhaust, automobile exhaust, and the ambient sample are very similar. The positions of the two Raman modes in these spectra are coincident to within $\pm 10 \text{ cm}^{-1}$ which is the estimated

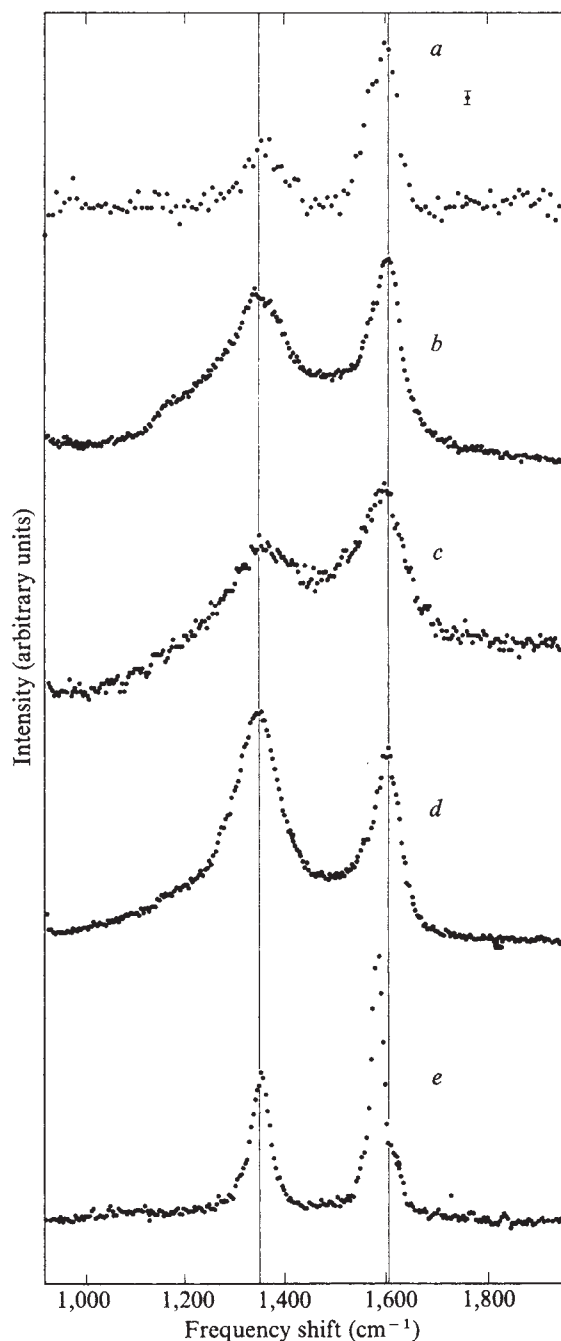


Fig. 2 Raman spectra between 1,200 and 1,700 cm^{-1} of a, ambient sample; b, automobile exhaust; c, diesel exhaust; d, activated carbon and e, polycrystalline graphite. The slit width for samples b–e was 3 Å; for sample a, 7-Å slits were used to improve signal to noise ratio.

experimental error. Since the phonon frequencies are a sensitive probe of the lattice, we suggest that these spectra give strong evidence for the existence of physical structures similar to activated carbon in the samples we have studied. This is not surprising since activated carbon is also produced in a combustion process.

We can estimate from literature data² the crystallite sizes in the various samples from the intensity ratios of the two observed Raman modes. The automobile exhaust and diesel exhaust samples have roughly the same peak intensity ratio, yielding crystallites of $\approx 50 \text{ Å}$ in size, while the ambient sample seems to have crystallite sizes of $\approx 100 \text{ Å}$. We would expect such structures to have very large internal surface area.

Novakov *et al.*⁴ have proposed that fine soot particles, which in many ways are similar to activated carbon, may have a major

role in atmospheric chemistry. To assess the importance of the proposed soot-catalysed reactions, it is important to determine the chemically active primary carbon in the carbonaceous fraction of ambient and source-enriched aerosol particles. Our results indicate that physical structures similar to activated carbon are present in diesel exhaust, automobile exhaust and ambient samples. The fact that these features tend to dominate the Raman spectrum may indicate that graphitic 'soot' is the major species in the samples we have measured. But, the large intensity in these modes may be due just to their large Raman cross-section, and therefore a quantitative interpretation of these results will have to await a more detailed analysis. Such an analysis will have to include measurements of the Raman cross-section, optical absorption cross-section, and take into account the little-understood particle size effects⁵.

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Fluctuations of seismicity before major earthquakes

LONG-TERM precursory changes of seismicity previously reported are (1) a change in the relationship between earthquake frequency and magnitude, and (2) a decrease in the frequency of micro-earthquakes. In a review of earthquake precursors Rikitake¹ cites eleven examples of the former and three examples of the latter. On the dilatancy hypothesis a decrease in activity is to be expected from dilatancy hardening²; an earlier gradual increase of activity due to the secular increase of tectonic stress was also postulated³. A more distinctive sequence of seismicity fluctuations can be recognised from data in seismological bulletins. The fluctuations are large: a burst of activity marking the start of the precursory sequence is followed by a period of abnormal quiet, and this lasts until the onset of the major event. We report here characteristic changes of minor earthquake activity, preceding a number of recent major earthquakes in regions with good seismographic coverage, and suggesting a new basis for long-term prediction relying directly on the normal data output of permanent seismograph networks.

The initiating burst of activity differs markedly from the major event: the general level of magnitude is substantially lower, and no earthquake is much larger than the rest. Thus the term 'precursory swarm' is appropriate, for although earthquake swarms are commonly regarded as characterising regions of Quaternary volcanism it is the lack of a main shock that distinguishes a swarm from a typical tectonic event. The abnormally low activity with which the precursory sequence continues defines a seismic gap in both time and space; the geographic gap is of premonitory value since the major event (as well as the precursory swarm) occurs within it, though whether it is well delineated depends on the ambient level of seismicity and the accuracy of epicentre location.

The phenomenon is illustrated by two major earthquakes, one from New Zealand and the other from California. The Milford Sound earthquake of 4 May 1976, magnitude $M_L = 7.0$, is the largest New Zealand shock since 1968, although by virtue of its location offshore in Fiordland, a rugged and sparsely

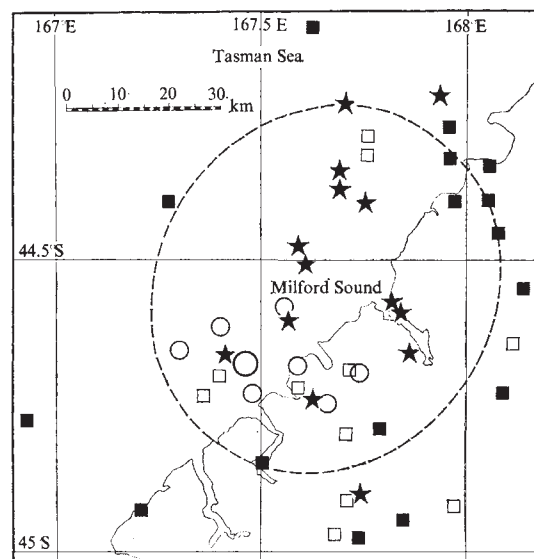


Fig. 1 Epicentre map of crustal earthquakes with $M_L \geq 4.6$, occurring from January 1961 to May 1976, and showing approximate boundary of precursory area for the Milford Sound earthquake of 4 May 1976, $M_L = 7.0$. The seismic episodes indicated are as follows: normal seismicity ($\square$), 1 Jan. 1961–21 Feb. 1968; precursory swarm ($\star$), 22 Feb. 1968–23 Dec. 1968; precursory gap ($\blacksquare$), 24 Dec. 1968–3 May 1976; major event ($\circ$), 4 May 1976–8 May 1976.

populated region, it attracted little public notice. The Ocotillo Wells earthquake of 9 April 1968, magnitude $M_L = 6.4$, was one of the two largest California earthquakes since 1954; it was widely felt and involved displacements along a 33-km segment of the Coyote Creek fault⁴.

The Milford Sound earthquake data are taken from published bulletins⁴, and from recent files made available by Dr R. D. Adams, Superintendent, Seismological Observatory, D.S.I.R., Wellington; the data for the Ocotillo Wells earthquake are taken from Hileman *et al.*⁵.

For the relevant areas, Figs 1 and 2 show the epicentres of located earthquakes occurring in the specified time intervals

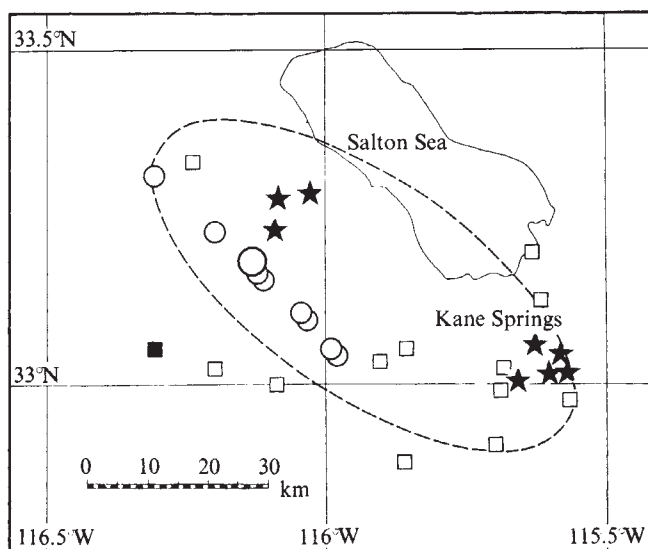


Fig. 2 Epicentre map showing approximate boundary of precursory area for the Ocotillo Wells earthquake of 9 April 1968, $M_L = 6.4$. 222 earthquakes with $M_L \geq 4.1$, occurring from January 1962 to April 1968 are shown. The seismic episodes indicated are as follows: normal seismicity ($\square$), 1 July 1962–10 April 1965; precursory swarm ($\star$), 11 April 1965–26 August 1965; precursory gap ($\blacksquare$), 27 August 1965–8 April 1968; major event ($\circ$), 9 April 1968–16 April 1968.

and magnitude ranges. (The Milford Sound major event was crustal in origin and earthquakes originating below the crust have been excluded.) Four seismic episodes are distinguished: normal seismicity, the precursory swarm, the precursory gap and the major event.

The hypothesis that all the swarm and major-event epicentres and none of the gap epicentres lie within a certain area is satisfied by the elliptical boundaries shown in Figs 1 and 2; in the Milford Sound example allowance is made for location errors of up to 7 km, which is within the typical standard deviation for epicentre locations in the region. Of course, any actual boundary will not be precisely elliptical. It is of interest, however, that in each example the orientation of the ellipse is approximately parallel to the dominant tectonic trend in the region.

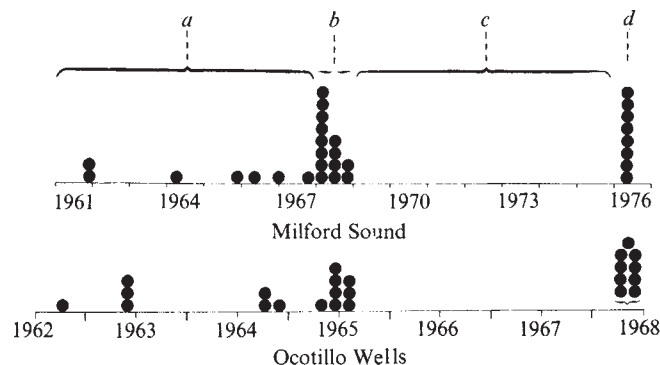


Fig. 3 Seismic sequences associated with the precursory areas of the Milford Sound and Ocotillo Wells earthquakes. The period of normal seismicity has been chosen about equal to that of the precursory gap, and the two time scales have been adjusted to facilitate comparison. *a*, Normal seismicity; *b*, precursory swarm; *c*, precursory gap; *d*, major event.

Thus the fluctuations of seismicity follow a simple geographic pattern. For the Ocotillo Wells sequence the precursory boundary encloses most of the normal seismicity and it is thus not surprising that the precursory gap episode is not represented by more epicentres.

The seismic sequences are plotted against time in Fig. 3, which shows how the seismicity within the precursory area fluctuates, in relation to the normal level, before a major event.

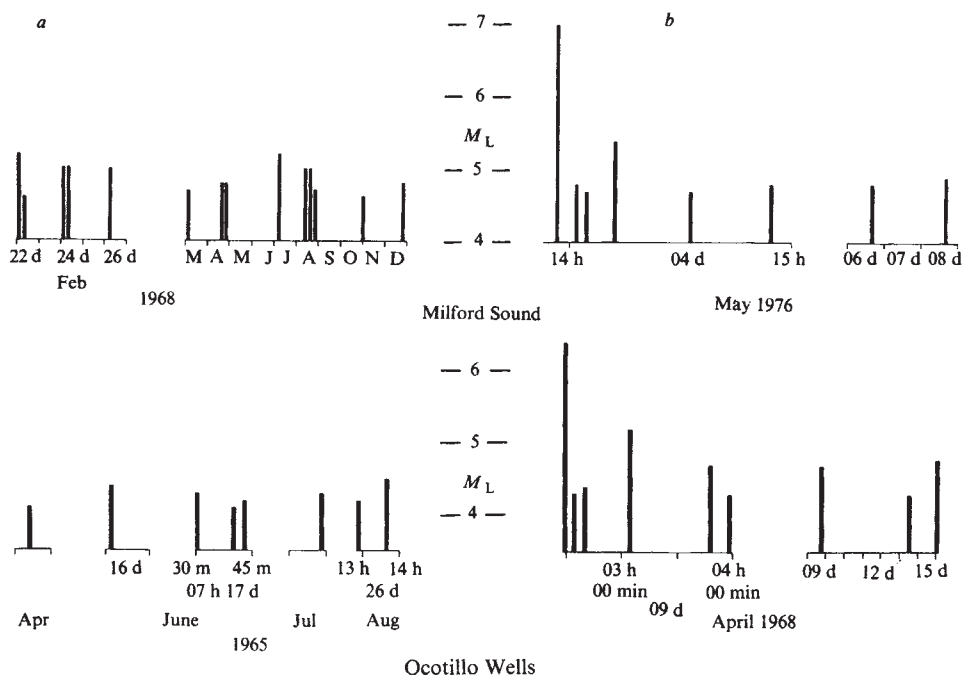


Fig. 4 Magnitudes of precursory swarm (*a*) and major event earthquakes (*b*). The time-scales are not uniform.

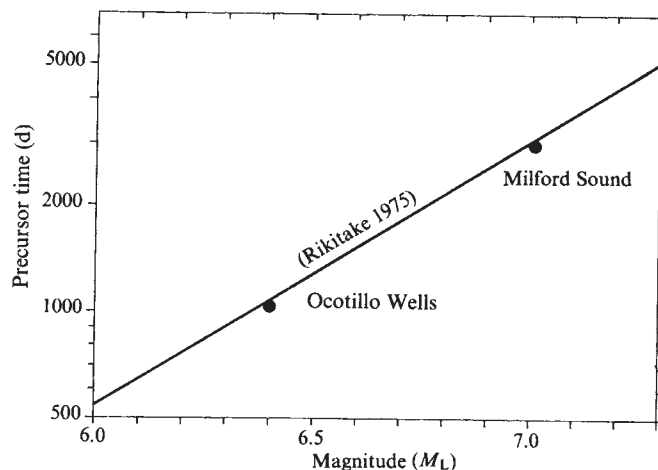


Fig. 5 Time interval between precursory swarm and major event, plotted against main-shock magnitude. Rikitake's curve is obtained from a plot of widely scattered data for eleven different types of precursory phenomena: land deformation, *b*-value, micro-earthquakes, source mechanism, fault creep, velocity ratio, velocity values, geomagnetic effects, resistivity, radon emission and oil flow.

The precursory swarm could be described as a rehearsal of the major event, but the gap is also an important feature of the precursor.

The premonitory value of the fluctuations of seismicity depends in the first instance on the successful recognition of a swarm as such. Magnitude level is no criterion as major events in the present sense of the term also occur at low magnitudes. The required criterion is provided by the distribution of magnitudes and, in particular, as mentioned above, by the absence of a main shock. This is illustrated in Fig. 4, which contrasts the two precursory swarms with the respective major events.

Taking the precursor time as the interval between swarm and major event (onset-to-onset) one obtains 2,994 d for the Milford Sound earthquake and 1,029 d for the Ocotillo Wells earthquake. These values are plotted against the magnitudes of the respective main shocks in Fig. 5. Also shown is the relationship obtained by Rikitake¹ based on other types of precursor.

The fluctuations of seismicity seem to have a physical origin closely related to that of the phenomena analysed by Rikitake. As with many of those phenomena, the dilatancy hypothesis offers an interpretation of the precursory swarm. For at the onset of dilatancy the rock undergoes pervasive cracking which in an inhomogeneous medium can be expected to involve a redistribution of stress, leading in some localities to an increase beyond the strength. But as the general effect of the cracking is to strengthen the rock, only comparatively minor earthquakes result at this stage. The mechanism of the well-known swarm activity in regions of Quaternary volcanism may be similar in essential respects, as this activity may also be associated with pervasive cracking as the rock cools and shrinks⁶.

A strategy of earthquake prediction has been suggested by Rikitake¹ in which an extremely long-range precursor would be identified by repeated geodetic surveys, and long-range precursors would then be sought by intensive geophysical methods. It now appears that fluctuations of seismicity may provide long-range precursory information from the normal output of a permanent seismograph network, without the use of intensive methods. Such methods could then be devoted to the search for short-term precursors.

Seismicity fluctuations have been identified in association with main shocks at magnitudes from 5.0 to 7.1. The phenomenon provides the following precursory information: the approximate location of the future major event is indicated at a prior time which is related to the magnitude of the main shock, and the area affected, although not always well defined, is also related to the magnitude. In addition, however, it seems that with the seismicity fluctuations the magnitude of the main shock increases with that of the swarm earthquakes: this relationship is potentially of great premonitory value and is now being investigated. Present studies are also leading to a detailed formulation of the characteristics of precursory swarms and to an assessment of the seismographic coverage required by the method at given levels of main-shock magnitude. On the basis of these studies the reliability of the method is being investigated preparatory to attempting actual predictions.

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Muon production of ^{92,94}Nb in the Earth's crust

ACTIVITIES due to long-lived ⁹²Nb ($t_{1/2} \approx 1.7 \times 10^8$ yr) and to ⁹⁴Nb ($t_{1/2} = 2.03 \times 10^4$ yr) in a refined bar of terrestrial niobium were discovered by Apt *et al.*¹. They speculated that the ⁹²Nb activity could have applications to chronologies of nucleosynthesis and to cosmogony. As an example, they calculated that their observed activity level would result if the isotopic ratio 4.7×10^9 yr ago were ⁹²Nb/⁹³Nb = 10^{-3} and if the half-life were 1.58×10^8 yr. More definite conclusions were difficult because the concentration expected today depends so strongly on the poorly known half-life, which they estimated to be 1.7×10^8 yr from a reactor irradiation. This sensitivity can be illustrated by noting that a 5% error in half-life corresponds after 4.7×10^9 yr to an error of a factor 2.74 in the anticipated activity. Quantitative calculations from galactic nucleosynthesis must therefore await a more precise measurement

of the half-life. Implications of primordial ⁹²Nb have recently been enlarged with the proposal² to use enrichments $\delta(^{92}\text{Zr})$ in the isotopic composition of Zr due to extinct ⁹²Nb to measure absolute time differences in the formation of meteorites and planets. If an initial ⁹²Zr/⁹⁴Zr ratio for each body can be obtained, differences between those initial values could be translated into time differences in the formation of the respective objects. We argue here that both projects are probably doomed to disappointment. It seems to us unlikely that the near equality in the two measured activities is a coincidence. They are respectively 0.058 ± 0.035 d.p.m. per kg (Nb) for ⁹²Nb and 0.32 ± 0.03 d.p.m. per kg (Nb) for ⁹⁴Nb. Such a result would be expected, for example, if both nuclei were created terrestrially over geologic time in the ratio of their activities, in this case in a production ratio $p(^{92}\text{Nb})/p(^{94}\text{Nb}) = 0.18 \pm 0.11$. We suggest that nuclear reactions following the capture of stopped cosmic-ray muons is the likely source, and we will show that both the magnitude of the activities and their relative strengths are consistent with this idea. Similar ideas have been developed by others, most notably to explain Xe anomalies in Te ores³.

Examination of a chart of stable nuclides shows that ⁹⁴Nb in this model arises from the reactions ⁹⁴Mo (μ^-, γ) ⁹⁴Nb, ⁹⁵Mo (μ^-, n) ⁹⁴Nb, ⁹⁶Mo ($\mu^-, 2n$) ⁹⁴Nb, ⁹⁷Mo ($\mu^-, 3n$) ⁹⁴Nb, ⁹⁸Mo ($\mu^-, 4n$) ⁹⁴Nb, and by ⁹³Nb (n, γ) ⁹⁴Nb, where the neutrons are regarded as arising from muon capture on all species in the Earth's crust. On the other hand, ⁹²Nb would arise from ⁹²Mo (μ^-, γ) ⁹²Nb, ⁹⁴Mo ($\mu^-, 2n$) ⁹²Nb, and so on. We use a theory of muon capture as developed by Singer⁴ in order to evaluate the various branchings following the muon capture. Molybdenum is the major target for direct production of Nb because charged-particle emission is much less probable than neutron emission. The major uncertainty in our results lies not in the theory, but in the unknown ancient history of the crustal rocks from which the Nb bar was purified. A time average of the Nb/Mo abundance ratio in these rocks enters, because only ⁹⁴Nb activity can be made by neutron capture on Nb whereas both Nb isotopes result from muon capture by Mo. A pure ancient Nb deposit, for example, would therefore contain only ⁹⁴Nb activity. Furthermore, the number of neutron captures by Nb per stopped muon depends on the chemical composition of the host mineral through its competition for the neutrons it produces. Apt *et al.* could not discover the history of the ores from which the Nb bar was refined, so we have calculated this competition for two idealised samples: (1) chondrite material, which presumably well represents the average heavy element abundances in the earth, and (2) typical terrestrial granites. Following Singer's description, we constructed a computer programme for calculating the distribution of neutron-emission multiplicities following muon capture on each relevant species, taking the surface-emission term to be 16%. Details of this calculation are given in ref. 5. For evaluating the absolute production, we took the muon stopping rate to be $100\text{--}150$ muons $\text{g}^{-1} \text{yr}^{-1}$ down to depths of about 10 m water equivalent⁶. If the ores were considerably deeper than this over the time-integrated production of the anomalous activities ($\sim 10^8$ yr for ⁹²Nb and $\sim 10^4$ yr for ⁹⁴Nb), the absolute activities would be considerably reduced.

Table 1 shows major features of our calculation. We assumed the so-called Z-law⁷—that the atomic capture of muons in a mixture is proportional to the nuclear charge Z of the competing atoms—enabling us to calculate in a given composition the fraction of stopping muons captured by each element. In Table 1, $\langle Z \rangle$ is the average charge for each of the two background compositions. The average number $\langle \nu \rangle$ of neutrons emitted per muon stopped is also calculated, as is the average neutron-capture cross section $\langle \sigma \rangle$ of the nuclei of each composition. These allow us to calculate the fraction of the neutrons captured by ⁹³Nb, taking its thermal cross section⁸ to be $\sigma = 1.15$ b. The compositional differences are dominated by the chondritic iron being much greater than granitic. The remaining entries in Table 1 show our calculated results for the numbers of each reaction occurring per muon

stopped in that sample. For the chondritic composition this process is well defined, but for the granitic case we have to assume values for the Mo/Si and Mo/Nb abundance ratios in the rock. We take the latter ratio to be the chondritic value Mo/Nb = 2.2, an assumption that affects the calculated $^{92}\text{Nb}/^{94}\text{Nb}$ production ratio. The very small ratio, Mo/Si, does not affect the $^{92}\text{Nb}/^{94}\text{Nb}$ production ratio as long as Mo/Nb is held at 2.2; therefore we take it also to be chondritic Mo/Si = 2.5×10^{-6} . Within these assumptions, which are easily scaled to other choices, Table 1 lists the production resulting from each stopped muon in the sample. If the granitic Mo/Si differs from 2.5×10^{-6} , the calculated entry for μ^- -capture reactions scales proportionately, and if Nb/Si differs from 1.15×10^{-6} , the calculated entry for ^{93}Nb (n, γ) scales proportionately.

Table 1 $^{92,94}\text{Nb}$ production per stopped muon

	Granitic	Chondritic
$\langle Z \rangle$ matrix	10.4	11.9
$\langle v \rangle$, neutrons per muon	0.43	0.54
$\langle \sigma(n, \gamma) \rangle$ matrix(b)	0.16	0.39
$^{97}\text{Mo}(\mu^-, 5n)^{92}\text{Nb}$	2.3×10^{-9}	1.4×10^{-9}
$^{96}\text{Mo}(\mu^-, 4n)^{92}\text{Nb}$	1.7×10^{-8}	9.9×10^{-9}
$^{95}\text{Mo}(\mu^-, 3n)^{92}\text{Nb}$	3.3×10^{-8}	1.9×10^{-8}
$^{94}\text{Mo}(\mu^-, 2n)^{92}\text{Nb}$	5.8×10^{-8}	3.3×10^{-8}
$^{92}\text{Mo}(\mu^-, \gamma)^{92}\text{Nb}$	4.7×10^{-8}	2.7×10^{-8}
Total ^{92}Nb per μ^-	1.6×10^{-7}	9.0×10^{-8}
$^{98}\text{Mo}(\mu^-, 4n)^{94}\text{Nb}$	2.8×10^{-8}	1.6×10^{-8}
$^{97}\text{Mo}(\mu^-, 3n)^{94}\text{Nb}$	1.9×10^{-8}	1.1×10^{-8}
$^{96}\text{Mo}(\mu^-, 2n)^{94}\text{Nb}$	1.0×10^{-7}	6.0×10^{-8}
$^{95}\text{Mo}(\mu^-, n)^{94}\text{Nb}$	1.3×10^{-7}	7.6×10^{-8}
$^{94}\text{Mo}(\mu^-, \gamma)^{94}\text{Nb}$	2.4×10^{-8}	1.4×10^{-8}
$^{93}\text{Nb}(n, \gamma)^{94}\text{Nb}$	7.8×10^{-7}	2.7×10^{-7}
Total ^{94}Nb per μ^-	1.1×10^{-6}	4.5×10^{-7}
$^{92}\text{Nb}/^{94}\text{Nb}$ per μ^-	0.14	0.20

Therefore, the granitic entries can be used more generally than for only the specific trace-element concentrations used in their calculation.

The calculated production ratios per captured muon, $p(^{92}\text{Nb})/p(^{94}\text{Nb}) = 0.14$ for granite and 0.20 for chondritic matter, bracket the steady-state production ratio 0.18 ± 0.11 needed to match the ratio of observed activities. Furthermore, the absolute concentrations are also about right. The observation¹ $^{92}\text{Nb}/^{93}\text{Nb} = 1.2 \times 10^{-12}$ translates in our model granite to 8.7×10^3 atoms ^{92}Nb (g granite)⁻¹. If interpreted as a steady-state concentration, this number must equal the product $1.6 \times 10^{-7} \tau(^{92}\text{Nb}) \lambda_\mu$, where the coefficient comes from Table 1 and λ_μ is the muon stopping rate per gram of granite per year. The required stopping rate, $\lambda_\mu = 222 \text{ g}^{-1} \text{ yr}^{-1}$, is about 50% greater than the value⁶ at a depth several metres water equivalent under the earth. Virtually the same stopping rate would be needed in chondritic material. The rough agreement in production ratio and in absolute yield attests strongly to the probable correctness of this explanation. Neutrons from other sources near the Earth's surface or from (α, n) reactions within the crust¹ may synthesise ^{94}Nb from ^{93}Nb , but the associated ^{92}Nb activity suggests that muons are a major source.

Major uncertainties exist in the history of the ore, of course, and these cloud firm conclusions. If deep material has risen to within 10 m from the surface, each activity within will have increased in time as muon reactions built the activity to saturation; however, since saturation requires roughly 10^8 yr for ^{92}Nb and only 10^4 yr for ^{94}Nb , time dependent effects can alter the activity ratio. There is also a major question of fractionation of Mo from Nb during the growth of these activities and the geologic processes leading to the mining sites. In pure Nb the $^{92}\text{Nb}/^{94}\text{Nb}$ activity ratio should be very small, whereas Table 1 shows in pure Mo it should be about 0.5. In principle,

such variations could yield interesting evidence of geologic history, because the activities of these two isotopes should differ in Nb samples purified from ores having different geologic histories. Searches for these activities in old molybdenum ores should prove interesting. It would also prove helpful if a Mo bar could be exposed to a sufficient flux of stopping muons to experimentally determine the ^{92}Nb and ^{94}Nb activities, for then our calculated sums of branching ratios could be replaced by experimental numbers, greatly improving the accuracy.

The idea that the ^{92}Nb could be a remnant of galactic p -process nucleosynthesis is of course an attractive hope. But, we find little grounds for optimism from p -process systematics. Most p -process nuclei seem to be produced as proton-rich progenitors, in which case ^{92}Nb is shielded by ^{92}Mo . The ^{92}Nb is similar to other heavy odd-odd nuclei ^{138}La and ^{180}Ta , both of which are very rare and may be taken as empirical guides to p -process nucleosynthesis in such cases. Their abundances are 10^{-1} to 10^{-2} of characteristic p -abundances in their neighbourhood. Taking the same estimate for ^{92}Nb leads to a total ever produced $^{92}\text{Nb}_{\text{total}} \sim 0.02$ to 0.002 per 10^6 Si, where we have estimated the average $N_p = 0.2$ by averaging ^{84}Sr , ^{94}Mo and ^{96}Ru , excluding ^{92}Mo which is known to be anomalously large. A photodisintegration-flow p -process calculation⁹ has recently yielded $^{92}\text{Nb}_{\text{total}} = 0.001$, an even lower estimate of total production. Our models of continuous nucleosynthesis suggest that about 2% of the total ^{92}Nb would have survived to the early Solar System; therefore $^{92}\text{Nb}_0 = 4 \times 10^{-4}$ to 4×10^{-5} per 10^6 Si, or $(^{92}\text{Nb}/^{93}\text{Nb})_0 = 3 \times 10^{-4}$ to 3×10^{-5} . This ratio could be enough to account for today's activity if $t_{1/2} \geq 1.7 \times 10^8$ yr, so again, one awaits a better half-life measurement. Even then, the expected amount is perhaps too small to expect to find $\delta(^{92}\text{Zr})$ anomalies due to extinct $^{92}\text{Nb}^2$.

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Particulate organic carbon in Atlantic surface waters

PARTICULATE organic matter (POM) in the oceans has a vital role in marine ecology as it is the major food source for living organisms in surface and deep waters. Nearly all of the suspended organic matter in the oceans originates from phytoplankton productivity in the euphotic layers and is comprised of living plankton and dead organisms (detritus). Because of the importance in the marine food web of suspended organic phases in seawater several investigations on their distribution and composition have been carried out^{1–3}.

Most of the available data, however, are based on sampling at a single location and hence the magnitude of latitudinal variation in the POM concentrations are not well established. Chester and Stoner⁴ have reported extensive measurements on the concentration of particulate organic carbon (POC) and particulate nitrogen (PN) in surface waters of the eastern Atlantic and Indian oceans. We present here results on the distribution of POC in the open ocean surface waters of the

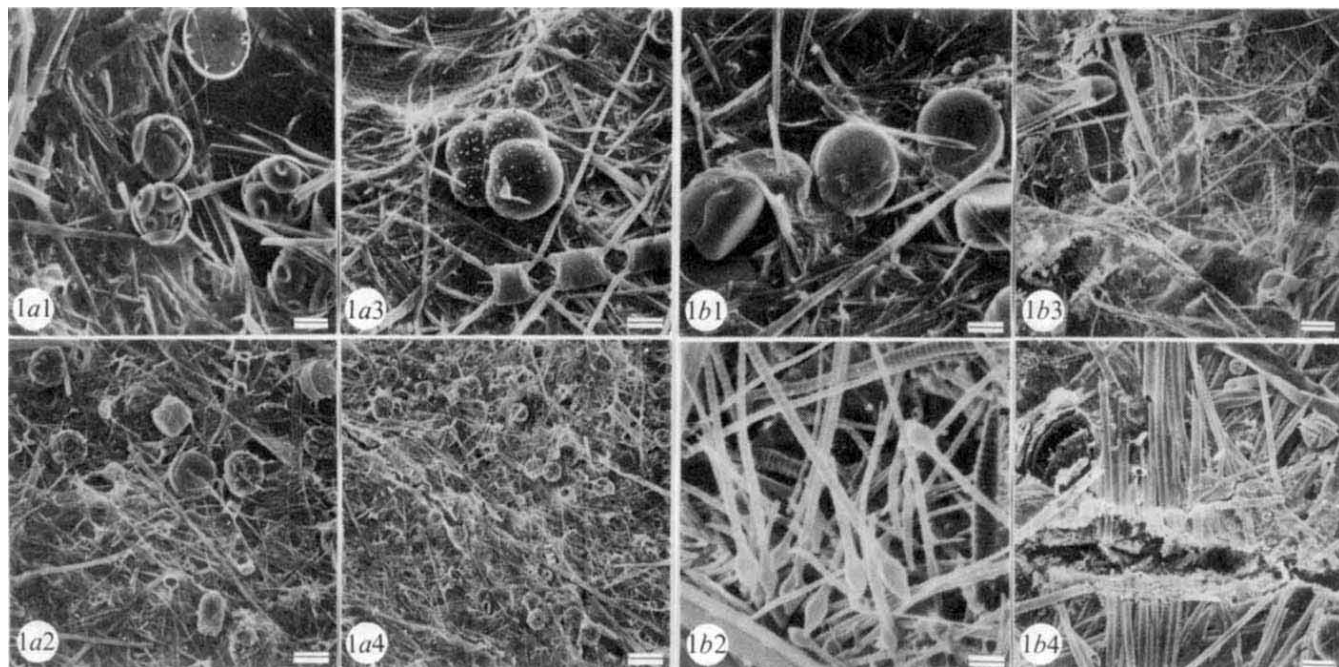


Fig. 1 Scanning electron microscope photomicrographs of particles trapped in the filters. Most of the particles in *a*, from the coast of Iceland and the Norwegian Sea, are calcareous (coccolithophorids and forams); the large circular particle on the top and the rod-like particles are siliceous. In *b*, from the Antarctic and the equatorial waters, the particles are mostly siliceous. Scale bars: *a1*, 5 μm ; *a2*, 10 μm ; *a3*, 10 μm ; *a4*, 20 μm ; *b1*, 5 μm ; *b2*, 5 μm ; *b3*, 20 μm ; *b4*, 20 μm .

Atlantic, between 72°N and 61°S; 60°W and 20°E, and its interrelation with primary productivity.

The samples were collected during the GEOSECS Atlantic expedition (July 1972–April 1973) by filtering large volumes (2,000–40,000 l.) of surface seawater while cruising between stations, usually 3° apart. Thus, the particles were trapped from representative samples of surface waters over hundreds of km. We used a cotton fibre filter with almost quantitative retention efficiency for particles > 5 μm and 60% for particles in the 0.5–1.2- μm range. The filter characteristics and filtration techniques are discussed in detail elsewhere⁵. The filters were rinsed with sufficient quantities of distilled water to remove sea salts, dried on board the ships at 90–100 °C, packed carefully and sent in poly-bags to shore-based laboratory for analysis. Figure 1 shows some of the trapped biogenic particles on the filter. The weight of total particulate matter (TPM) (the weight difference in the filter before and after the experiment) trapped per filter was 0.1–3.0 g. The samples were ashed at 400–425 °C, and the weight loss on ashing was attributed to POM. Particulate organic carbon content of the samples was calculated by assuming that it constitutes 50% of POM (ref. 7). The calculated particulate organic carbon is designated as CPOC henceforth.

The TPM and CPOC concentrations in surface waters ranged between about 10–600 and 2–170 $\mu\text{g kg}^{-1}$, respectively, and are strongly interrelated (Fig. 2). The latitudinal distributions of TPM and CPOC concentrations (Fig. 3) are similar, with pronounced maxima near subpolar regions (~60°N and 60°S) and low concentrations in the tropics and mid-latitudes (30°N–40°S).

The relation between TPM and CPOC for the surface Atlantic suspended phases in different latitudinal belts are given in Table 1. The mean TPM/CPOC for the Atlantic (72°N–61°S; 60°W–20°E) is 3.94, corresponding to a mean CPOC content of ~25%, that is, ~50% POM. The remaining ~50% of TPM is composed of biogenic skeletal remains, (CaCO_3 and opal) and terrestrial materials (aluminosilicates, quartz). The TPM/CPOC ratios exhibit geographical variations (Table 1, Fig. 2). For samples from northern subpolar regions (45–72°N) the mean ratio is (3.57 ± 0.38) compared to a value of (4.8 ± 0.7) for samples from 45–61°S. The samples from the 45°N–45°S region have the lowest TPM/CPOC ratio, $3.15 \pm$

0.18. The observed TPM/CPOC ratios are in good agreement with results of Chester and Stoner⁴. The differences in the TPM/CPOC ratios in various regions seem to be due to variations in the elemental composition of biogenic populations

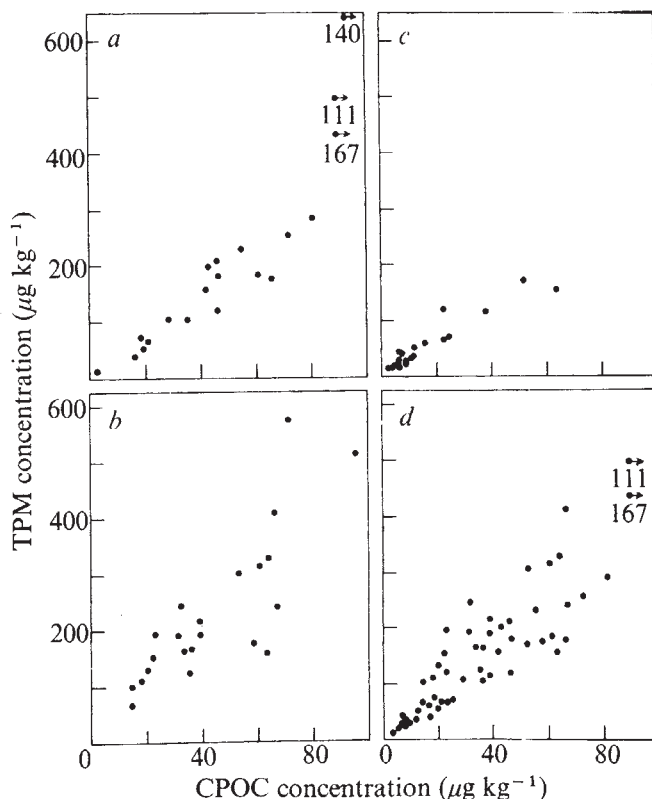
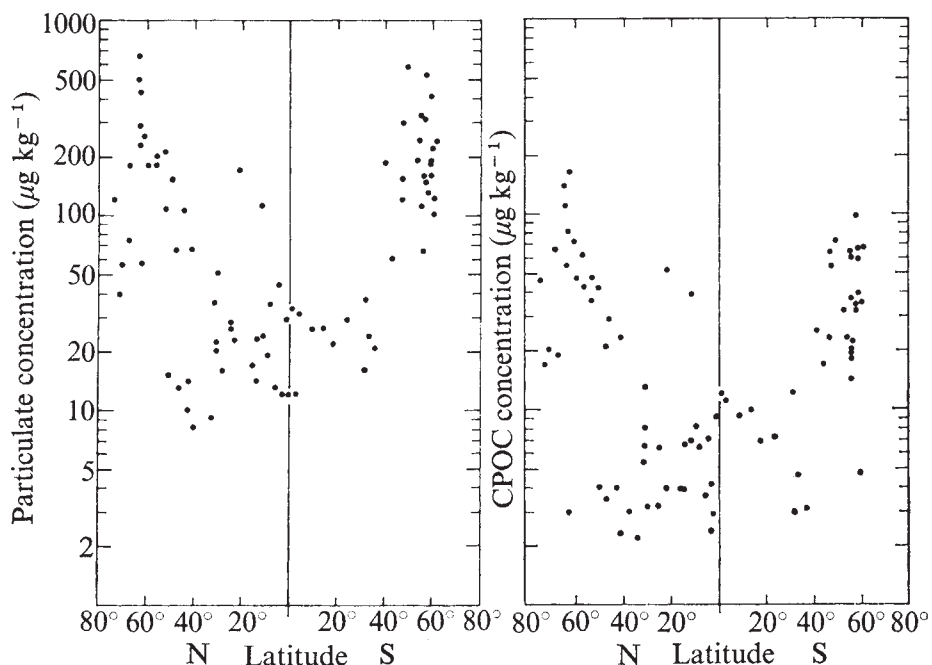


Fig. 2 Correlation diagram for the TPM–CPOC concentrations for various regions of the Atlantic surface waters. The linear correlation between TPM and CPOC is evident. Note that CPOC constitutes about 20% of TPM in samples from Antarctic circumpolar region compared to ~30% for rest of the Atlantic. Only samples having ≥ 200 mg weight loss during ashing were taken to avoid possible uncertainties due to weightloss of filter during filtration. *a*, 72°–45°N; *b*, 45°–61°S; *c*, 45°N–44°S; *d*, 72°N–61°S.

Fig. 3 Latitudinal distribution (72°N–61°S) of TPM and CPOC in Atlantic surface waters. The distribution patterns for both TPM and CPOC are almost identical, with pronounced maxima in the subpolar regions due to high organic productivity. Low concentrations have been observed for waters between 30°N and 30°S.



occurring in these bands. Our detailed analyses⁸ indicate that siliceous tests dominate in the Antarctic circumpolar waters (40°–60°S) whereas calcareous tests are relatively more abundant in the North Atlantic (Fig. 4).

The regional differences in the CPOC concentrations of surface waters can be roughly correlated with nutrient supply due to upwelling and phytoplankton activity. In the North Atlantic, high CPOC concentrations were observed in the Denmark Straits and off the coast of Iceland, where upwelling of nutrient-rich waters caused by passage of strong currents over the Iceland–Faroes Ridge occurs, and in the Canary Islands, where cool nutrient-rich water ascends to the surface due to off-shore wind action⁹. Similarly, CPOC concentrations are high south of the Antarctic Convergence zone, where very high primary productivity has been observed due to upwelling of circumpolar waters. Lowest CPOC concentrations

are in the western Atlantic, between 30°N and 30°S. Our results have the following implications: (1) Organic biological matter constitutes ~50% by weight of the total suspended matter in the Atlantic Ocean. (2) Organic carbon in sediments constitutes only ~0.3% compared to a value of ~25% in surface particulates. This suggests that most of the organic carbon produced in surface waters dissolves within ocean water. (3) The mean residence time of particulate organic carbon within the top (100–200-m) layer against consumption by dissolution and grazing is deduced to be about 5–10 d. This is based on the ratio of the standing crop of particulate carbon (from our measurements in surface waters) and its primary production rate¹². The standing crop of particulate organic carbon, $\Sigma\text{POC} = C_s L$, where C_s is the surface concentration and L is the mean concentration depth, the depth over which the concentration decreases by a factor of e . The

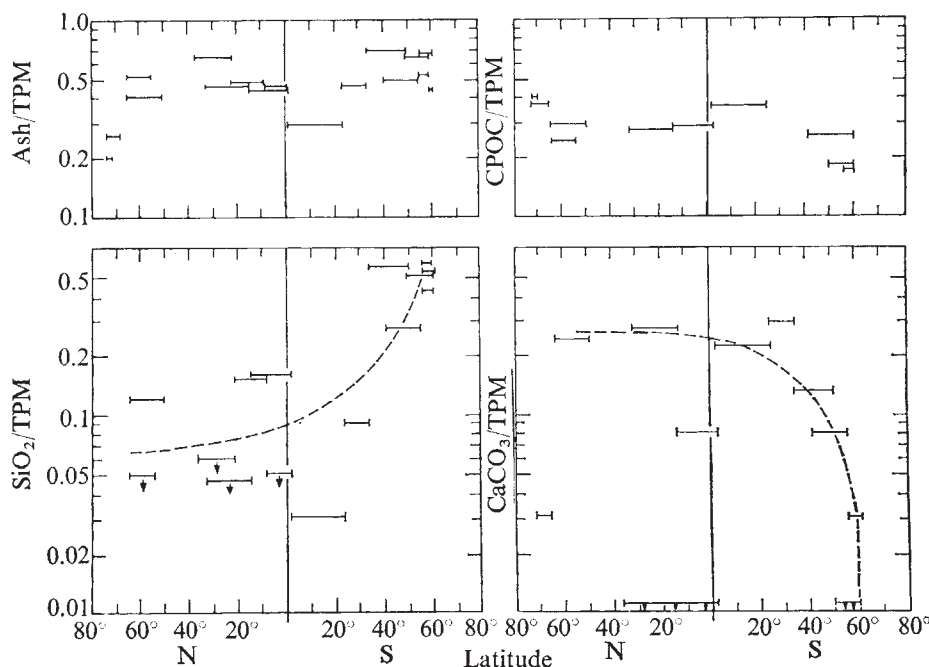


Fig. 4 Latitudinal variation of the ash, CPOC, CaCO_3 and SiO_2 contents of TPM from surface Atlantic waters. The CaCO_3 is relatively more abundant in the northern latitudes, whereas samples from ~60°S contain mainly siliceous organisms.

Table 1 TPM, CPOC interrelation for surface Atlantic waters in various latitudinal belts

Latitudinal belt	No. of samples	CPOC concentration ($\mu\text{g kg}^{-1}$)		TPM-CPOC relation* ($m \pm \Delta m$)	C	Correlation coefficient for TPM-CPOC relation
		Range	Mean			
72°N–45°N	19	17–167	59	(3.57 $\pm$ 0.38)	0.9	0.92
45°N–45°S	28	3–52.5	12	(3.15 $\pm$ 0.18)	3.8	0.96
45°S–61°S	22	14.5–96	44	(4.8 $\pm$ 0.7)	20.3	0.81
72°N–61°S	69	3–167	35	(3.94 $\pm$ 0.25)	10.2	0.89

*TPM = ($m \pm \Delta m$) CPOC + C, where TPM and CPOC are their concentrations in $\mu\text{g kg}^{-1}$ and C is a constant.

value of ΣPOC for the (45°N–45°S) belt in the Atlantic is calculated to be about $60 \mu\text{g cm}^{-2}$ using a value of $12 \mu\text{g kg}^{-1}$ for C_s (Table 1) and 50 m for L (refs 12, 13). Primary production rate, P , in this region¹⁴ is about $100 \text{ mg m}^{-2} \text{ d}^{-1}$. The consumption time, τ_c ($\tau_c = \Sigma\text{POC}/P$) of particulate organic carbon in these regions is thus estimated to be about 6 d. The corresponding value for the Atlantic surface waters (72°N–61°S) is ~ 9 d, using $C_s = 35 \mu\text{g kg}^{-1}$, $L = 50$ m and $P = 190 \text{ mg C m}^{-2} \text{ d}^{-1}$. The estimated value for τ_c refers to both living and dead organisms. The mean survival time for living organisms is much smaller, about 1–2 d, as the ratio¹ of living phytoplankton to detritus is approximately 1:6.

(4) The average SiO_2/CPOC molar ratio in particles from the circumpolar waters ($\sim 60^\circ\text{S}$) is about 0.4. Thus in the Antarctic polar front, biological productivity (primarily siliceous organisms) converts 0.4 mol of soluble silica into suspended phases per mol of carbon. Biogenic silica constitutes more than 90% of the total particulate silica at 50–60°S.

(5) The non-uniform distribution of the TPM and CPOC concentrations suggests that horizontal mixing due to surface currents is not effective in homogenising the particle concentrations; the sinking rates of these suspended phases, therefore, must be faster than the surface current velocities. As most of the CPOC ($\sim 95\%$) dissolves in the water column before being deposited as sediment, the trace elements associated with particulate organic carbon phases are also expected to be injected in seawater in dissolved form. If so, the dissolution flux of elements could also have geographical dependence governed by primary productivity in various latitudinal bands. The dissolution flux of elements associated with the hard skeletal part of the organisms (for example, CaCO_3 and opal) will similarly show geographical variation, as the CaCO_3/TPM and SiO_2/TPM ratios vary considerably in surface waters.

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Nickel in komatiites

THE principle of partitioning of trace elements between magma and crystalline phases is an extremely useful tool in deciphering the origin and evolution of magmas. With our present knowledge of partition coefficients calculations usually assume them to be constant. The nickel contents of suites of komatiitic lavas from South Africa, the evolution of which is controlled by olivine fractionation, suggest that the partition coefficient for nickel between olivine and liquid is not constant, but increases from <3 for liquids with $>20\%$ MgO and $>1,000$ p.p.m. Ni to 11 for liquids with 10% MgO and 200 p.p.m. Ni. There are two fundamentally different views on the origin of basic magmas. O'Hara¹ proposed that the mantle melts to produce a picritic liquid which undergoes extensive olivine fractionation prior to eruption. The alternative model, summarised by Ringwood², assumes that basic magma is a direct product of melting and undergoes no fractionation. Ringwood's rejection of the fractionation hypothesis is

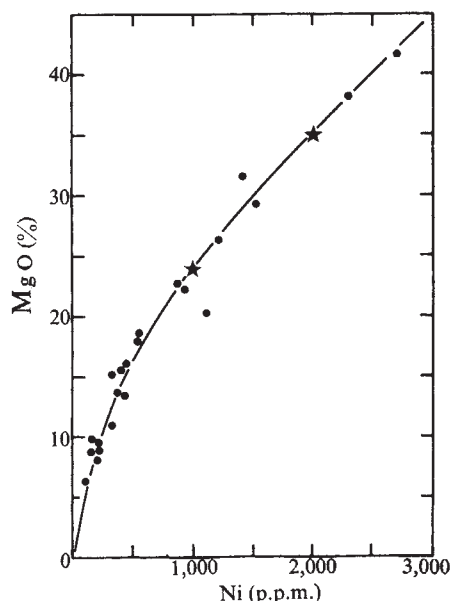


Fig. 1 Plot of Ni against MgO contents of komatiites analysed in Table 1. Stars denote proposed parental magma compositions.

based largely on calculations of the Ni content of magmas². All his calculations assume a constant partition coefficient for Ni between olivine and liquid in the range 12–15. Several recent investigations concluded that K_D is not constant but that it decreases (1) with increasing temperature^{3,4}; (2) with increasing MgO content in the liquid⁵; (3) with increasing Ni content in the liquid⁶, and (4) as crystallising olivines become more forsteritic⁷. These effects have been reviewed in detail elsewhere⁸ but the net effect is that for a liquid, rich in MgO and Ni, crystallising a forsteritic olivine at high temperature, K_D may be significantly lower than the figure currently accepted. Komatiitic lavas fall perfectly into this category of liquid as they have high MgO and Ni contents and it has been shown experimentally⁹ that they crystallise very magnesian

olivines at temperatures well above the liquidus for normal basalts. Most of the studies which have indicated low K_D values have involved experimental work on synthetic samples⁴⁻⁷, some of which⁵⁻⁷ were iron-free and hence, although they represent an extremely important step towards understanding partition coefficients, quantitatively the K_D values may be suspect. We have analysed the Ni contents of komatiites with a wide range of compositions to determine the partition coefficient for these seldom-erupted lavas to test more rigorously the constraints imposed by Ni values on the fractionation model for basic magmas.

Table 1 MgO and Ni in komatiites and calculated degrees of fractionation

Sample no.	MgO (%by weight)	Ni (p.p.m.)	Olivine removed*	
			Model 1	Model 2
S3	18.46	529	51	17
S7	15.75	407	55	23
S11	15.96	424	55	23
S16	13.69	383	58	27
S28	17.93	512	52	18
OV3	13.57	423	56	27
OV4	11.09	348	58	31
OV5	9.76	169	60	34
SG3	20.38	1102	48	11
SG80	22.28	935	45	6
VB1	15.45	337	56	24
VB4	9.83	179	59	34
V11	6.37	107	63	38
40J	8.08	205	62	36
53J	31.64	1407	17	C
87J	22.98	862	43	4
88J	26.58	1203	35	C
R16	41.58	2716	C	C
AUS	29.36	1533	25	C
VU32a	38.13	2298	C	C
LV4	9.40	210	60	34
LV7	8.50	205	61	35

C indicates MgO content is higher than in the theoretical parental magma used in the calculations and hence is regarded as a cumulus-enriched rock. S3-S28 from Anhaeusser (unpublished), OV3-OV5 from ref. 11, SG3-LV7 from ref. 10.

*F, proportion of liquid remaining is $(100 - \% \text{ olivine removed})/100$.

The geological relations for most of the komatiites chosen for analysis (from the Barberton Mountainland in South Africa) have been described elsewhere¹⁰. All the samples are demonstrably lavas; as indicated by pillow structures, vesiculation or spinifex textures; except sample 53J which is the chilled margin of a dyke. Their MgO and Ni contents are given in Table 1 (complete major element analyses have been published for most samples (refs 10, 11 and C. R. Anhaeusser, unpublished)). The values are calculated on an H_2O^+ -free basis (Fig. 1), and a very close correlation between Ni and MgO is apparent. It has been suggested^{10,12} that these samples are related by olivine fractionation, and hence for these suites of lavas we have an opportunity to study the variation in Ni content produced by the removal of olivine.

Green *et al.*⁹ have suggested that komatiitic samples containing 35% MgO represent liquids while McIver¹² and Cawthorn and McIver¹³ believe such compositions to be cumulus-enriched in olivine and that the true liquids contain significantly less than this. Here we interpret the data using two hypothetical parental magmas, one with 35% and the other with 24% MgO. Figure 1 suggests that such liquids contain 2,000 p.p.m. and 1,000 p.p.m. Ni respectively. The olivine composition which crystallises from these magmas is approximately Fo_{93} which contains 51% MgO (ref. 9). Starting with parental magmas containing 35% and 24% MgO it is possible to calculate the degree of olivine fractionation required to produce the MgO contents of residual liquids with the MgO values given in Table 1. These calculated degrees of fractionation are also listed in Table 1: models 1 and 2 referring to parental magmas with 35% and 24% MgO respectively.

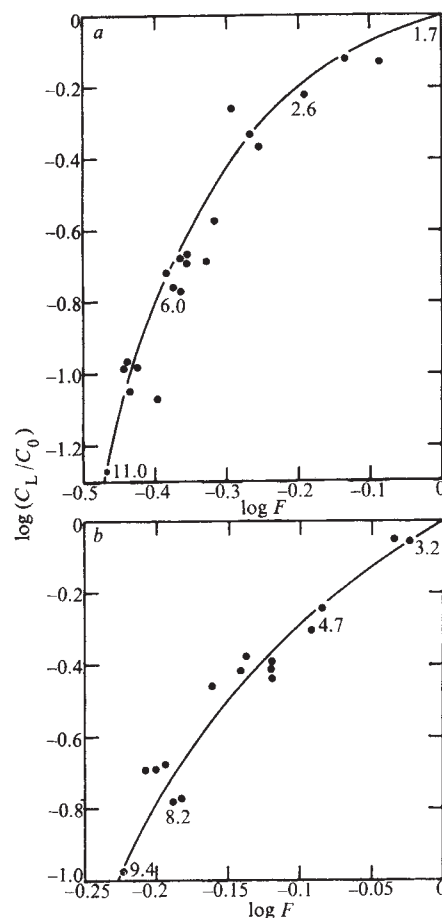


Fig. 2 Plot of $\log(C_L/C_0)$ against $\log F$. Slope of graph is $K_D - 1$ (as shown in text) and values for K_D are given at various points. *a*, Data for model 1 which assumes the parental magma contains 35% MgO and 2000 p.p.m. Ni. *b*, Model 2 for a parental magma with 24% MgO and 1,000 p.p.m. Ni.

The Rayleigh fractionation law states $C_L/C_0 = F^{K_D - 1}$ where C_0 is the trace element content of the parental magma, C_L that of the differentiated magma; F the proportion of differentiated magma produced, and K_D the partition coefficient. This may be rewritten as $\log(C_L/C_0) = (K_D - 1) \log F$.

Assuming 2000 p.p.m. (model 1) and 1000 p.p.m. Ni (model 2) for C_0 and having calculated the value for F from Table 1 we can plot a graph of $\log(C_L/C_0)$ against $\log F$ (see Fig. 2) and this will give a slope of $K_D - 1$. It is readily apparent from Fig. 2 that the graphs are not linear and hence the partition coefficient cannot be constant. The slope of the curves has been calculated at various points and the value for K_D , derived from the slopes, included in Fig. 2. Considering the model proposed by Green *et al.*⁹, the initial slope of the curve is 0.7 and hence K_D is 1.7. (It is interesting to note that the experimentally determined K_D of Green *et al.*⁹ is only 2.1 and hence agreement between experiment and these calculations on natural samples is extremely good.) At the extreme end of differentiation considered here, for liquids containing 6.37% MgO, the K_D as calculated from the slope of the graph is 11. Alternatively, if we consider model 2 the initial partition coefficient for liquids containing 24% MgO is 3.2 and has a maximum value of 9.4. Pyroxenes may begin to crystallise from magmas with low MgO contents. Hence, it may be that some of the most differentiated liquids of this study are not the product of fractionation of olivine alone. The K_D values determined for these low MgO liquids may not therefore apply to olivine: liquid partitioning, but this will not qualitatively alter the arguments presented here.

The values for the partition coefficient for low MgO-liquids ($< 8\%$ MgO) are fairly close to those predicted for basic magma¹⁴. Hence, for such compositions the partition coefficients determined

for these komatiites and other magmas appear compatible. For the MgO-rich compositions, however, the values are very much lower.

With reference to the debate between Ringwood and O'Hara mentioned earlier we conclude for the partition coefficients calculated here that: (1) the primary picritic magma envisaged by O'Hara¹ may contain very much higher nickel contents than suggested by Ringwood² because the partition coefficient is much lower. And (2) the rate at which nickel will be extracted from this parental magma by olivine fractionation will be slower than anticipated by Ringwood². Specifically, it is apparent from Table 1 that an initial magma containing 24% MgO and 1000 p.p.m. nickel may undergo 40% olivine fractionation to produce a residual liquid with 6% MgO and 100 p.p.m. nickel—values perfectly compatible with those of typical basic magmas. O'Hara¹ does not quantify his melting and crystallisation models, but these figures presented above suggest that the variation in partition coefficients makes his models qualitatively more tenable.

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Rhythm perception in early infancy

THE chief characteristic of rhythm perception is the subjective grouping of objectively separate events. In a rhythmic sequence of identical tone-bursts, adults do not perceive the repetition of a single sound, but a recurring configuration which has temporal form. Such a sequence is organised according to the Gestalt law of proximity^{1,2}. Organisation of temporal form has never been studied systematically in pre-verbal infants. We present here results suggesting a precocious achievement of this function and contrasting with previous research³ which failed to demonstrate organisation of spatial form by babies in accordance with the proximity law.

We adopted an habituation paradigm in which infants received auditory reinforcement contingent upon their visual fixation on a simple patterned-figure: a black outline-square on a white background. The infants themselves initiated the presentation of sound by looking at the figure and terminated it by looking away. After several such fixations, the auditory reinforcement was changed from one sound sequence to another. Any resulting increase in time of fixation on the visual stimulus was an index of discrimination.

Sequences of tone-bursts were presented by a loudspeaker placed directly behind the stimulus figure at a distance of 40 cm from the infant. The tone-bursts, 40 ms in duration, were derived from a tape-recording of a consonant chord produced by an electronic organ, with 270 and 1,620 Hz as dominant frequencies; intensity was 63 dB, about 25 dB above the ambient noise level. The stimulus figure subtended a visual angle of 8° and was positioned 20° to the left of midline. Fixation, as assessed by the corneal reflection technique⁴, was observed from directly in front

of the infant, through a small hole in the screen containing the figure. The infant was judged to be fixating when, his eyes being turned to the left, the stimulus reflection was clearly observable over the right of the pupillary opening. Duration of fixation, to the nearest tenth of a second, was recorded manually by a switch which simultaneously operated sound-emission and an event-recorder. In previous research, a high inter-observer reliability has been obtained for this measure⁵.

The first experiment was designed to demonstrate discrimination between the rapid, quite different sequences, S1 and S2, shown in Fig. 1. A regular pulse of tone-bursts, S1, was changed to an irregular sequence, S2. The two sequences had the same mean density of sound. We tested two samples, each of 10 infants, with mean ages of 71 d (s.d. 12) and 107 d (s.d. 6) respectively. Three

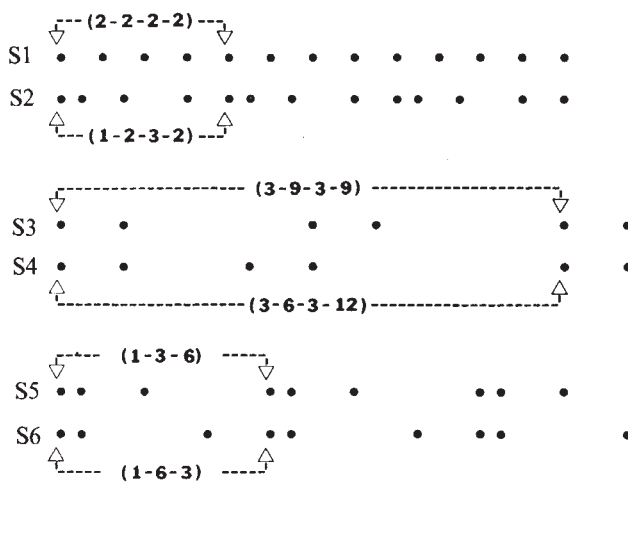


Fig. 1 Sound sequences. Each dot represents a 40-ms tone-burst. The shortest onset-to-onset interval was calibrated as 97 ms. All intervals were multiples of this unit. Their relative magnitudes in each sequence are given in brackets. Arrows delimit the period of each sequence. For example, the period of S2 is a succession of 1, 2, 3 and 2 time units (that is 97, 194, 291 and 194 ms). A sequence started always at the beginning of its period, and terminated when visual fixation ended (experiment 1) or after completion of the period in progress at that instant (experiments 2 and 3). Scale bar represents 1 s.

fixations without sound reinforcement were followed by 12 fixations reinforced by S1 and then three fixations reinforced by S2. Median fixation times are shown in Fig. 2a. A significant increase in fixation time followed the change in reinforcement ($F = 10.37$, $P < 0.005$), indicating discrimination of the two sequences. No main or interaction effect was associated with age.

In a second experiment, we studied discrimination of slower rhythms, using the sequences S3 and S4 depicted in Fig. 1. The visual fixations of 10 infants (mean age 69 d; s.d. 18) were contingently reinforced nine times by S3 and then three times by S4. Fixation time increased ($t = 3.72$, $P < 0.005$) when S4 replaced S3 (Fig. 2a). Thus, the 6-unit intervals of S4 were discriminated from the 12-unit intervals of S4 or from the 9-unit intervals of S3; alternatively, a new ratio of intervals was detected in S4. In any case, we conclude that infants are able to perceive intervals of six units (582 ms) as subjective links between sounds.

The aim of the third experiment was to examine perception of temporal form in sequences differing only in the order of their intervals. In the preceding experiment, discrimination might be attributed solely to the detection of a new interval. In experiment 3, however, the same intervals were used in both sequences, and the minimum segment for distinguishing between them was composed of a pair of successive intervals. Thus, the grouping of three consecutive sounds into a perceptual configuration was mandatory if discrimination was to occur. The longest interval appearing in S5 and S6 (Fig. 1) had already been shown to be

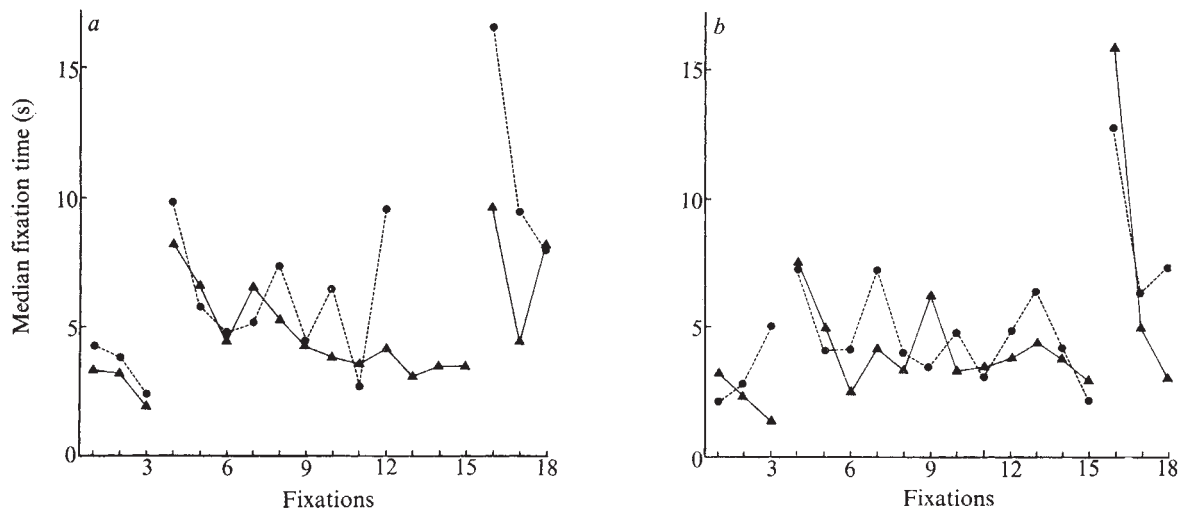


Fig. 2 *a*, Median time of fixation in experiments 1 and 2. In experiment 1 (▲), there was no sound reinforcement for fixations 1–3. S1 was presented contingently with fixations 4–15, and S2 with fixations 16–18. In experiment 2 (●), there was no sound reinforcement for fixations 1–3. S3 was presented contingently with fixations 4–12, and S4 with the final three fixations. The duration of the first fixation after change of reinforcement was compared with the mean duration for the preceding three fixations. *b*, Median time of fixation in experiment 3. No sound reinforcement was associated with fixations 1–3. For Group 1 (●), S5 was presented contingently with fixations 4–15 and S6 with fixations 16–18. For Group 2 (▲), the order of sequence presentation was reversed. The duration of fixation 16 was compared with the mean duration for fixations 13, 14 and 15.

perceptible in experiment 2. Therefore, within each reinforcement, all the sounds may have been linked in a temporal continuum. The first interval in each sequence was the same in order to ensure that discrimination was not based solely on a difference in this first interval, without further grouping. To adults, the sequences sound like recurring groups of three pips, the groups (. . .) in S5 being perceived as the inverse of the groups (. . .) in S6. In all emissions of S6, however, the first and final groups were incomplete (see Fig. 1). We tested two samples, each of 10 babies. Group 1 (mean age 69 d; s.d. 12) was tested in the order S5 followed by S6, and Group 2 (mean age 70 d; s.d. 18) was tested in the reverse order. Median fixation times are shown in Fig. 2*b*. An increase in fixation time followed the change in sequence ($F = 11.81$, $P < 0.005$); order of testing was associated with no reliable main effect or interaction. Since the differentiating of these sequences entails the grouping of three successive sounds, we infer that they were perceived as recurring 'rhythmic groups' organised in temporal form according to the Gestalt law of proximity. In addition, it may be noted that, following the first half-second, the rhythms can be distinguished only by the order of the within-group intervals. The magnitude of the novelty response suggests that, rather than perceiving only a single, very brief change, the infants have also noted the repetitive difference in within-group structure.

A succession of several sounds was apprehended by babies as a psychological unit. This phenomenon of temporal grouping is, of course, not peculiar to rhythm perception. Language comprehension, for example, requires a similar process, since a semantic unit must be grasped as a whole, despite its sequential character. In the results reported here, perceived structure rests on a purely temporal variable: the relative values of the intervals between sounds. These results indicate that skills of temporal analysis and synthesis, prerequisites for operating with the sequential dimension of language, are present well before the stage of speech, and suggest that the early experience of time is more complex than is generally assumed.

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The whalebill is a stork

THE avian order Ciconiiformes contains a heterogeneous assemblage of long legged, long necked birds which have traditionally been classified together because of superficial resemblance. The order usually contains the storks, ibises, herons and two rather aberrant birds, the whalebill (*Balaeniceps rex*) and the hammerkop (*Scopus umbretta*), which are placed in monotypic families, the Balaenicipitidae and Scopidae, respectively. The evolutionary relationships among the members of the Ciconiiformes and between this order and other living birds are little understood. Using an analysis of the morphology of the stapes (the single avian ear ossicle)^{1,2}, I have obtained evidence for the evolutionary affinity of the whalebill with the storks, which now seem to form a monophyletic assemblage.

The whalebill, whalehead or shoebill (Aves: *Balaeniceps rex*) is a strange, storklike bird with an enormous swollen head and a hooked beak. It is restricted to marshes and riverine situations in eastern Africa from the southern Sudan to Zambia. It is largely nocturnal, and feeds on various vertebrates including frogs, snakes and even lungfishes, but also molluscs and carrion. It has many similarities with the true storks (including bill clattering behaviour), but its systematic position has always been uncertain. Recently it has been thought to have more similarities with the pelecaniform birds (order Pelecaniformes), while the resemblance to storks was thought to be superficial³. The characters used, however, were not analysed on the basis of primitive and derived states.

Study of the morphology of the stapes, or columella, makes possible a reassessment of the evolutionary affinities of the whalebill and the storks. The stapes is of great evolutionary significance as sequences of primitive to derived characters can be established beyond reasonable

doubt. The typical avian stapes is reptilian, with a flat footplate and a straight bony shaft emanating from the centre of the footplate. Several avian groups, however, have unique, derived stapedial morphologies. I have assumed that: (1) the stapes found in most birds (most of the non-passerines and the suborder Passeres of the Passeriformes, which I now restrict to a separate order Passeriformes^{1,2}) is homologous with the same element in reptiles, and represents a retained primitive condition, and (2) where pockets of derived stapedial morphologies occur, they indicate evolutionary relationships, unless there are compelling reasons to assume that convergent evolution has occurred.

I have examined the stapes of the whalebill (*Balaeniceps*), 23 species of herons (13 genera), 10 species of ibises (8 genera), and 11 species of storks (9 genera), including the small form, *Ciconia abdimii* (75 cm long), to avoid anatomical effects due to allometric growth; most storks are large birds. I have also studied the stapes of the monotypic family Scopidae, which contains the equally enigmatic hammerhead or hammerkop (*Scopus umbretta*), a species also confined to Africa south of the Sahara. All specimens were from the collections of the US National Museum and the University of Michigan.

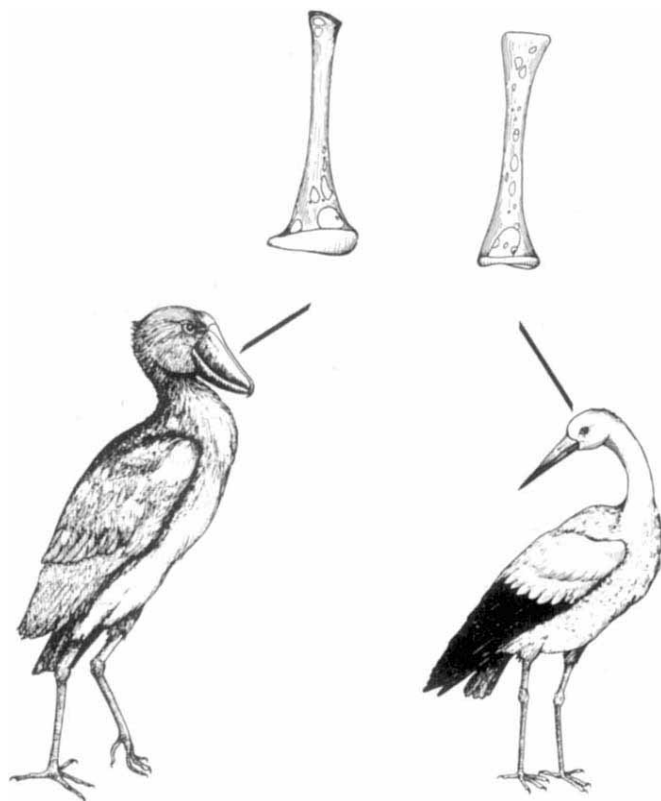


Fig. 1 Left, the whalebill (*Balaeniceps rex*), and right, the white stork (*Ciconia ciconia*), with lateral views of their stapes or columellae above; stapes drawn to the approximate same scale. The proximal ends are lower. Drawn by Ms Melissa Marshall.

I found that all the herons (Ardeidae, including the boat-bill, *Cochlearius cochlearius*), all the ibises (*Threskiornithidae*) and *Scopus* (Scopidae) have the primitive condition of the stapes, thus revealing nothing of their phylogenetic relationships, while all the storks and the whalebill have an identical, derived stapedial morphology. Pelecaniform birds have various stapedial morphologies that will be described in detail later together with those of the groups considered here, but they are quite different, elongate, somewhat curved structures. The stapes of the storks and whalebill (Fig. 1), here termed the stork stapes, is characterised as a broadly tubular structure that enlarges slightly at

the footplate region, and exhibits numerous fenestrae along the entire surface, usually with one or several large openings at the base near the footplate. Such a derived stapedial morphology common to the storks and the whalebill is interpreted as compelling evidence that the storks as defined at present are monophyletic and that the whalebill (*Balaeniceps*) is derived from them. Some authors⁴ have made a case (primarily on osteological grounds) that the storks and New World vultures (Cathartidae) are closely allied; however, all of the cathartids possess the primitive stapedial morphology.

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Early viral functions of *in* (ts)-1501 temperature-sensitive SV40 mutant

TEMPERATURE-SENSITIVE (ts) virus mutants have been useful in defining virus–host interactions in SV40 productive and transforming infections. We have isolated an SV40 ts mutant, *in*(ts)-1501, by extracellular mutagenesis, using ultraviolet radiation of wild type (WT) SV40¹. The mutant, which has properties different from previously described SV40 ts mutants^{2,3}, is activated from its integrated state in nonpermissive transformed cells at temperatures above 39 °C and is capable of productive infection in permissive cells at elevated (conditional) temperatures¹. Many properties of the 1501 mutant are analogous to the early ts cI mutants of bacteriophages in which a heat-inactivated protein cannot maintain the stable integration of the prophage in the bacterial chromosome at elevated temperatures^{4–8}. This analogy suggested that maintenance of SV40 DNA integration in transformed cells requires an early viral function, that is, before the inception of viral DNA replication. Therefore we have investigated the effect of the *in* gene mutation on two other early virus functions—stimulation of host-cell DNA synthesis and tumour (T)-antigen synthesis.

TsA mutants, the only previously identified mutants mapped in the early region of the SV40 genome⁹, show normal induction of host-cell DNA synthesis at 40 °C, but some show a reduced induction at 42.5 °C (ref. 10). We studied stimulation of host-cell DNA synthesis in 1501 ts mutant-infected and WT SV40 strain 777-infected confluent TC7 cells. TC7 is a continuous line of African green monkey kidney cells that is permissive for SV40 productive infection¹¹. The results (Table 1) indicate that the 1501 mutant can induce host-cell DNA synthesis at both conditional and nonconditional temperatures.

SV40 T-antigen, a nonstructural virus-coded protein, is expressed in the nuclei of productively and abortively infected and transformed cells. Approximately 30–40% of the SV40 genome is represented by this protein, the molecular weight of which has been estimated to be 70,000–100,000 (refs 12 and 13). The T-antigen is the SV40 *A* gene product, as defined by the tsA group of SV40 mutants^{13–17}. Although Brugge and Butel¹⁸ found that the synthesis of T-antigen was not temperature-sensitive in tsA-transformed or productively infected cells, Robb *et al.*¹⁴ showed that cells productively and abortively infected by these mutants had decreased T-antigen expression at the conditional temperature, and Osborn and Weber¹⁵ found that T-antigen decreased with time at the elevated temperature in tsA-transformed cells. Tegtmeyer *et al.*¹³ found that, at the conditional temperature, the tsA mutants had an increased turnover of

Table 1 Induction of cellular and viral DNA synthesis in TC7 cells infected with wild type and *in(ts)*-1501 virus

Incubation temperature (°C)	Mock-infected		WT SV40-infected		1501-infected	
	Precipitate (c.p.m. per 10 ⁵ cells)	Supernatant (c.p.m. per 10 ⁵ cells)	Precipitate (c.p.m. per 10 ⁵ cells)	Supernatant (c.p.m. per 10 ⁵ cells)	Precipitate (c.p.m. per 10 ⁵ cells)	Supernatant (c.p.m. per 10 ⁵ cells)
37	1,101	27	34,892	9,450	38,923	12,850
41	1,572	101	26,750	13,867	37,872	10,667

Cells, growing in 60-mm Petri dishes, were maintained in Eagle's minimal essential medium supplemented with 2 mM glutamine and 2% heat-inactivated (56 °C, 30 min) foetal bovine serum. Cell cultures were incubated in dark, water-saturated, 5% CO₂, temperature-regulated incubators. Virus was adsorbed for 1 h at 37 °C, followed by the addition of medium and then incubation at either 37° or 41 °C. The cells were labelled 20 h after infection with ³H-dT (0.5 µCi ml⁻¹ specific activity 6.7 Ci mmol⁻¹, New England Nuclear) for 90 min. DNA was selectively extracted by the method of Hirt²⁶. The Hirt precipitate consisted of cellular DNA and the supernatant consisted of viral DNA. All determinations are average counts from triplicate Petri dishes.

T-antigen and an altered intracellular distribution in both productively infected and transformed cells at the elevated temperature. Tenen *et al.*¹⁶ and Alwine *et al.*¹⁷ found that T-antigen induced by *tsA* mutants is more thermolabile than that induced by WT virus.

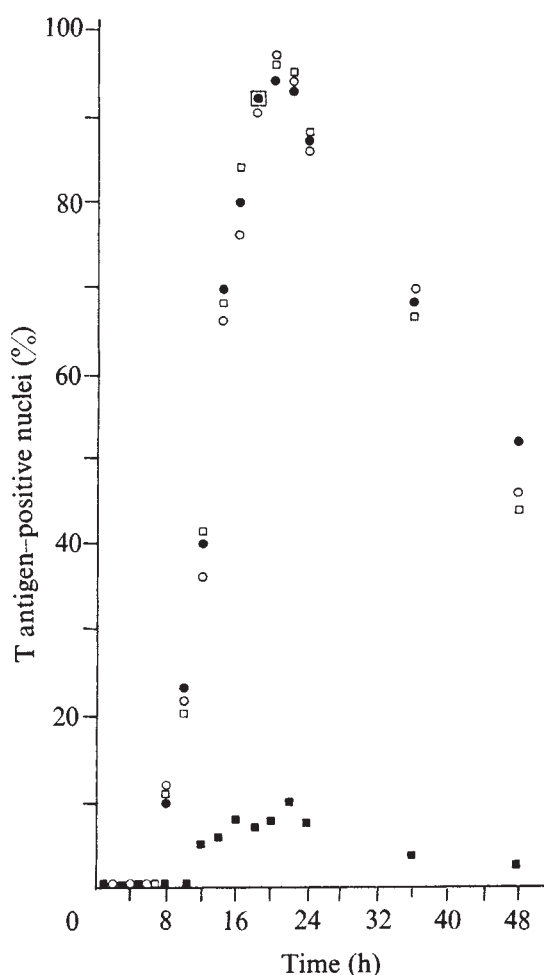


Fig. 1 Monolayers of African green monkey kidney cells (TC7) growing on coverslips in 60 × 15-mm plastic Petri dishes were infected with a multiplicity of infection of 10 by either wild type or *in(ts)*-1501 virus. After adsorption of the virus for 1 h, medium was added to the plates. Those cells infected with WT virus were incubated at 37 °C (○) or 41 °C (●). Plates with 1501-infected cells were also incubated at 37 °C (□) or 41 °C (■). Each point represents the percentage of T-antigen-positive nuclei determined in 2,000 cells. Cells, fixed on coverslips, were stained for 30 min with hamster T-antiserum (Flow), diluted 1 : 10 in phosphate-buffered saline (PBS), and rinsed for 30 min in PBS. They were then incubated for 30 min at 37 °C after addition of 5 drops of fluorescein-conjugated rabbit anti-hamster IgG, diluted 1 : 10 in PBS, were added to each coverslip. The coverslips were then washed in PBS, mounted on glass slides with 1 drop of PBS-glycerine 1 : 10, pH 7.4, and examined with a Leitz fluorescence microscope. Each point represents the average of two experiments.

We studied T-antigen formation in WT SV40 and 1501 productively infected TC7 cells using a modification of the indirect immunofluorescence technique described by Pope and Rowe¹⁹. After virion adsorption at 37 °C for 60 min, T-antigen development was monitored in WT SV40-infected and 1501-infected cells incubated at 37 °C and 41 °C (Fig. 1). More than 90% of the WT SV40-infected cells at both temperatures and 1501-infected cells at 37 °C showed positive T-antigen fluorescence, but less than 10% mutant-infected cells were T-positive at 41 °C.

We also studied the effects of elevated temperature on T-antigen expression in WT SV40-transformed and 1501-transformed hamster kidney cells. The histories and characteristics of T8-AP1, a hamster kidney cell line transformed by WT SV40, and HK10-c2 (*in(ts)*-1501), a twice-cloned, heat-inducible

Table 2 Determination of T-antigen in cell extracts by antibody absorption

Incubation mixture	Titre
Buffer	1 : 8
WT SV40-transformed cell (37 °C)	0
WT SV40-transformed cell (41 °C)	0
1501-transformed cell (37 °C)	0
1501-transformed cell (41 °C)	1 : 8

Subconfluent cultures were grown at 37 °C and 41 °C for 48 h. T-antigen was extracted by the method of Ahmad-Zadeh *et al.*²⁷. Cells were suspended at concentrations of 10⁷–10⁸ in 5 ml of extraction buffer (2.5 mM Tris-HCl, pH 7.4, 0.5M LiCl, 1 mM EDTA), sonicated three times for 15 s, and immediately centrifuged for 30 min at 30,000g and 4 °C. The supernatant was removed and used as the antigen. Extracts were adjusted to the same protein concentration (20 mg ml⁻¹). Antigen was assayed by the ability of the cell extract to absorb antibody to T-antigen. A modification of the method of Alspaugh *et al.*²⁸ was used. Equal volumes of anti-T serum and the cell extracts were incubated at 37 °C for 60 min, then at 4 °C for 16 h. Incubation mixtures were then serially diluted and assayed for unbound T-antibody by indirect immunofluorescence on WT SV40-transformed cells. The titre represents the highest dilution of the incubation mixture that still gave the characteristic nuclear speckling of T-antigen-positive cells.

hamster kidney cell line transformed by 1501, were described previously³. Because Robb²⁰ showed that WT SV40-transformed and *tsD*-transformed 3T3 cells have reduced T-antigen expression at nongrowing saturation densities, we monitored T-antigen in subconfluent (60–70%) cultures. Unlike WT SV40-transformed cells, the 1501-transformed cells had decreased T-antigen expression at the elevated temperature (Fig. 2). Increasing activation of infectious virus was observed in parallel cultures of 1501-transformed cells at 41 °C but not at 37 °C nor in WT SV40-transformed cells at either temperature.

The presence of T-antigen was also assayed by using antigen extracts from each cell line grown at 37 or 41 °C to absorb the T-antibody from SV40 T-antiserum before staining for immunofluorescence (Table 2). If T-antigen was present in the extract, it would bind to the T-antibody and prevent immunofluorescent staining of WT SV40-transformed cells. The immunofluorescence titre was decreased eightfold or greater by the extracts from 1501-transformed cells grown at 37 °C and

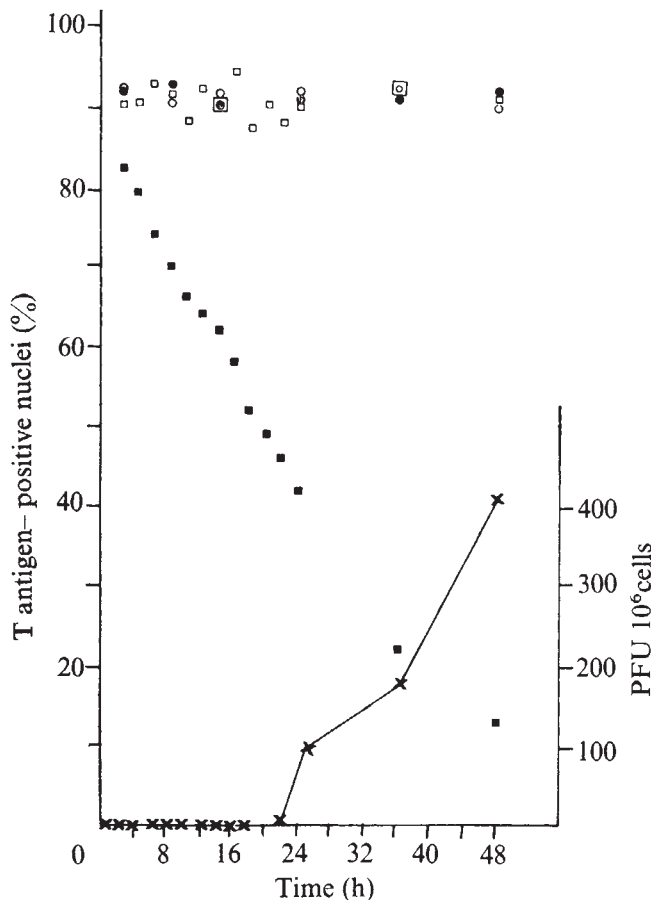


Fig. 2 All cell lines were maintained at 37 °C for 24 h after passage. At time zero, WT-transformed cells were incubated at 37 °C (○) and 41 °C (●). Parallel cultures of *in(ts)*-1501-transformed cells were incubated at 37 °C (□) and 41 °C (■). Infectious virus (×) activated at 41 °C in 1501-transformed cells was assayed as plaque-forming units (PFU). The percentage of T-positive cells was determined as described in the legend of Fig. 1. The cell viability, measured by Trypan blue exclusion, remained more than 92% throughout the experiment. *in(ts)*-1501-transformed cells exhibited a characteristic decline in viability after 96 h at 41 °C.

from T8-AP1 grown at either temperature; however, the extract from 1501-transformed cells grown at 41 °C did not absorb the antibodies in the T-antiserum, indicating that T-antigen is not present in these conditions.

Thermal lability of the 1501 T-antigen extract was assayed by heating aliquots of the extract for various times at 50 °C. Using the antibody-absorption technique described in Table 2, we found that T-antigen was completely inactivated after 30 min at 50 °C.

We tested for the reversability of the apparent loss of T-antigen in HK10-c2(*in(ts)*-1501) cells at the nonconditional temperature. Subconfluent cultures of cells, maintained at 41 °C for 24 h, were shifted to 37 °C. The percentage of T-antigen-positive nuclei gradually increased from 38% after 24 h at 41 °C to 90–95% after incubation at 37 °C for 3 d. Cell viability, measured by trypan blue exclusion, remained greater than 90% throughout the experiment.

These results suggest that the *in* gene affects the heat lability of T-antigen and that certain antigenic determinants of T-antigen may be required for the maintenance of SV40 DNA integration. Furthermore, induction of host-cell DNA synthesis and T-antigen are separate early viral functions. We postulate that one function of the SV40 T-antigen may be to interact with specific recognition sites on either viral or cellular DNA, selectively regulating viral DNA integration and/or late viral DNA transcription. Consistent with this hypothesis are the

findings of Carrol *et al.*²¹, who demonstrated that SV40 T-antigen binds strongly to double-stranded DNA with two different salt-concentration-dependent affinities, and of Reed *et al.*²², who showed that T-antigen can bind selectively to SV40 DNA at or near the origin of SV40 DNA replication.

We must reconcile our observations with findings that the T-antigen is the *A*-gene protein^{13,16,17,23}. The thermal lability of T-antigen from 1501-transformed cells indicates a relationship between the 1501 and *tsA* mutants. The most likely explanation is that the *in* and *A* cistrons may code for a multifunctional protein, such as that found in the *hisB* gene in *Salmonella typhimurium*²⁴ or the aspartokinase I-homoserine dehydrogenase I gene of *E. coli*²⁵, in which two activities can be altered independently. Other explanations are possible, however. A test of the hypothesis of T-antigen pleiotropy will necessitate the isolation and characterisation of the mutant T-antigen and study of its interaction with DNA.

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Contiguity to male foetuses affects morphology and behaviour of female mice

DURING studies on the role of gonadal hormones in aggressive behaviour of mice, we observed large variations in both the morphology and behaviour of females. At birth, variation was evident with respect to the principal external sex-differentiating marker—distance between the anus and the genitals, with some females being difficult to distinguish from males. Moreover, a significant proportion of females, upon reaching adulthood, were more responsive to androgen than others, exhibiting male-like aggressive behaviour more quickly following its administration. These observations led to the speculation that a certain proportion of females had been masculinised naturally during prenatal

development. We present here data which show that such masculinisation does occur and that it is mediated by proximity to male foetuses.

That prenatal masculinisation of the female can occur naturally in the rodent was suggested by the data of Clemens¹. Based upon a relatively small sample, especially with respect to that used to assess behaviour, it was reported that female rats, contiguous to male foetuses during gestation, had larger ano-genital distances at delivery and displayed more male sex behaviour in response to androgen treatment given in adulthood than did females that had not been in such close proximity to males. It was suggested that masculinisation of the female was mediated by exposure to androgen from the foetal testis. We now present data which show conclusively that, in mice, the position of the female in the uterus relative to that of males determines the extent to which the female is both morphologically and behaviourally masculinised.

Thirty-eight 60–70 d-old nulliparous Rockland-Swiss albino mice, housed separately in 11 × 7 × 5-inch translucent cages, were provided with food and water in excess and kept on a 12 h light/12 h dark cycle with lights on at 0600 h. An adult male was introduced into each female's cage and removed on the discovery of a copulatory plug. Pregnancy was interrupted at 2000 h on day 18 of gestation (delivery normally occurs between 0100 and 0500 h on day 19 of gestation, taking the day of coitus as day 0 of pregnancy) and the foetuses were delivered surgically. The adult was killed by cervical dislocation, the uterine horns were exposed, and the foetuses expelled with their position in the uterus relative to other foetuses noted. They were cleaned with saline and ano-genital distances measured. The females then were gonadectomised under ether anaesthesia and marked by injecting India ink into the footpads. The sequence of marks identified the position of a foetus with respect to the sex of the foetuses on either side. Males from 10 of the pregnant animals also were gonadectomised and marked. The animals then were fostered in same-sex groups of four or five to mothers that had delivered within the preceding 24 h and whose young had been removed.

The animals were weaned on day 21 of life and kept in their foster-littermate groups until day 60, when they were implanted subcutaneously with a 10-mm Silastic capsule containing 5 mg testosterone (T) and housed singly. Testing for aggression, begun 2 d later, was conducted on alternate days for a maximum of 50 d (25 tests) or until a fight occurred. Testing consisted of placing an adult olfactory bulbectomised male into the cage of each female and leaving it there for 10 min. Olfactory bulbectomised males, although eliciting aggression comparable to that of intact males, neither initiate fights nor respond to attack by retaliating. Thus, they provide a relatively constant stimulus for tests of aggression². A fight was scored when an animal chased and bit the stimulus male. The number of days of T exposure required to induce aggression was recorded. Although the administration of T to non-neonatal androgen-exposed adult mice will produce aggression, animals exposed to T during early development will fight sooner following the start of T exposure in adulthood³.

Fifty-two females survived to adulthood: 15 had been situated between two male foetuses (group 2M), 28 next to one male foetus (group 1M), and nine contiguous with no male foetus (group 0M). Nineteen males also survived to adulthood. An analysis of variance of the ano-genital distances of the females recorded at delivery yielded a significant uterine position effect ($P > 0.001$) (see Fig. 1). Individual comparisons using Duncan's test⁴ with α at 0.05 showed that animals of group 2M had significantly larger ano-genital distances than did those of group 1M and 0M. The latter two groups did not differ from one another. As it was possible that the absolute number of males in the uterus rather than contiguity to males mediated the effect upon ano-genital distance, an analysis of covariance was performed with the number of males per uterus serving as the covariate. This analysis revealed that ano-genital distance did not vary as a function of the absolute number of males present in a uterus. The mean ano-genital distance for each of the 3 groups of females was then compared to the mean for the males using Dunnett's test⁴ to compare means to a standard with α at 0.05. Males had a significantly larger mean ano-genital distance than did any of the groups of females.

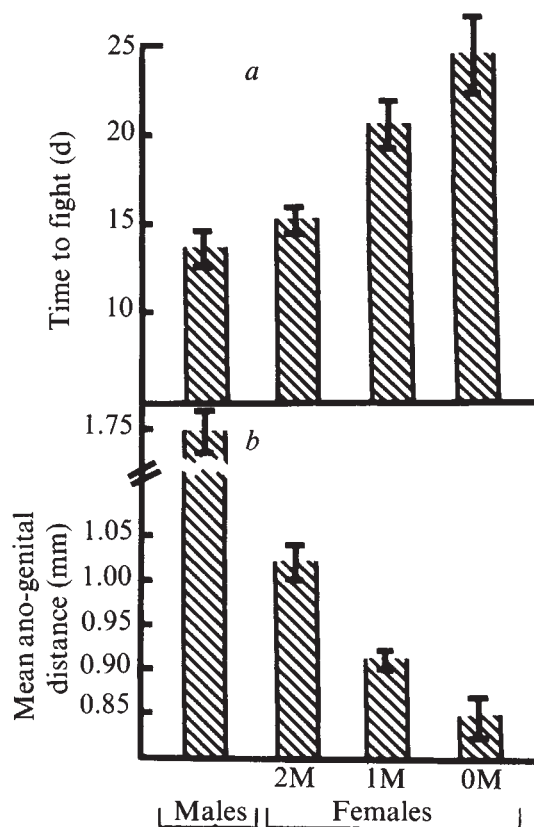


Fig. 1 *a*, Number of days to fight following the start of testosterone exposure of male and female mice, and *b*, ano-genital distance of delivery. Females were located in the uterus either between two male foetuses (2M), next to one male (1M), or contiguous to no male foetus (0M). All animals were delivered approximately 3.5 h prematurely and gonadectomised at that time. Data are means $\pm$ s.e.m.

As ano-genital distance varied as a function of contiguity to male foetuses, it was predicted that the females of the most morphologically masculinised group (2M), with the largest ano-genital distance, would require the shortest period of exposure to T in order to establish aggression. Conversely, females of the least masculinised group (0M) would require the longest exposure period. These predictions were supported. Females of Group 2M did require a significantly shorter period of exposure to T to exhibit aggression than did animals of group 0M. Females of group 1M were intermediate, not differing significantly from the animals of group 2M and 0M. The males did not differ significantly from the females of group 2M and 1M but did require a shorter exposure period to T than animals of group 0M. Finally, collapsing across the three groups of females, a significant negative correlation ($r = -0.30$, $P < 0.05$) was obtained between ano-genital distance at delivery and the number of days of T exposure required to induce aggression.

The variability normally exhibited by female mice in morphology and behaviour can thus be accounted for, in part, by the position of the female in the uterus relative to that of males. Females situated between two male foetuses were masculinised as indicated by larger ano-genital distance and increased responsiveness to the aggression-promoting property of T. Females contiguous with one male were masculinised with respect to behavioural responsiveness to T but not morphologically. Female rat foetuses contiguous to a male foetus are heavier⁵, so the large ano-genital distance of female mice situated between two males might have been due to the fact that these females were heavier than the others. This is not the case, however, as there were no differences in body weight between the three groups of females. It also is possible that the effect is specific only to the Rockland-Swiss strain. Although data on the effect of uterine position on responsiveness

to T are not available, we have found that uterine position does significantly influence ano-genital distance in the CF-1 strain.

The foetal mouse testis begins to secrete androgen on day 12.5 of gestation⁶, and tritiated T injected into the amniotic fluid of a rat foetus passes by diffusion into the amniotic fluid of a contiguous foetus⁷. This indicates, therefore, that the effect upon female morphology and behaviour of proximate male foetus may be mediated by exposure to androgen and that its transmittal occurs locally at the level of adjacent amniotic membranes.

Studies of the difference between disparate groups provide fundamental information concerning factors which affect development, as in the use of males and females to demonstrate the influence of gonadal hormones. Identifying the determinants of differences between individuals, however, is a prime requisite for understanding the variability within a group and, therefore, should be one of the principal concerns of psychology. Our study seems to identify a contributory factor underlying the development of individual differences.

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Mutagenicity and toxicity of visible fluorescent light to cultured mammalian cells

MANY cultured mammalian cells are characterised by karyotypic instability, high rates of spontaneous transformation and high frequencies of background mutation. The toxicity of visible light for mammalian cells¹⁻⁴ is usually attributed to photochemical reactions between light and the culture medium, and riboflavin, tryptophan and tyrosine are often thought to mediate this toxicity¹⁻³. Light has been shown to produce strand breaks in DNA^{5,6}. Because many tissue culture operations are conducted under fluorescent light, we have investigated whether the toxicity and DNA strand-breaking activity of light are accompanied by mutagenicity. We report here that this is the case.

The toxicity of fluorescent light for V-79 Chinese hamster lung (CHL) cells incubated during irradiation in either complete α -MEM (CM) or balanced saline solution (BSS) is shown in Fig. 1. Both survival curves are slightly shouldered, implying a saturable repair process. Evidently light is toxic to these cells whether they are irradiated in CM or BSS, although toxicity after 2 h of irradiation is greater for cells in CM. This result is in contrast to those of Stoen and Wang², who found no killing of human D98/AH2 cells irradiated with fluorescent and near-ultraviolet light in phosphate-buffered saline.

We tested whether pre-irradiation of CM, toxic for some cells^{2,7}, would kill V-79 cells subsequently incubated in it. Table 1 shows that medium that has been pre-irradiated for 3 h in the same conditions as the cells does not reduce the colony-forming ability of V-79 cells. The final colony diameter after 1 week of growth, however, was decreased and the cellular morphology was altered by pre-irradiated CM (Table 1).

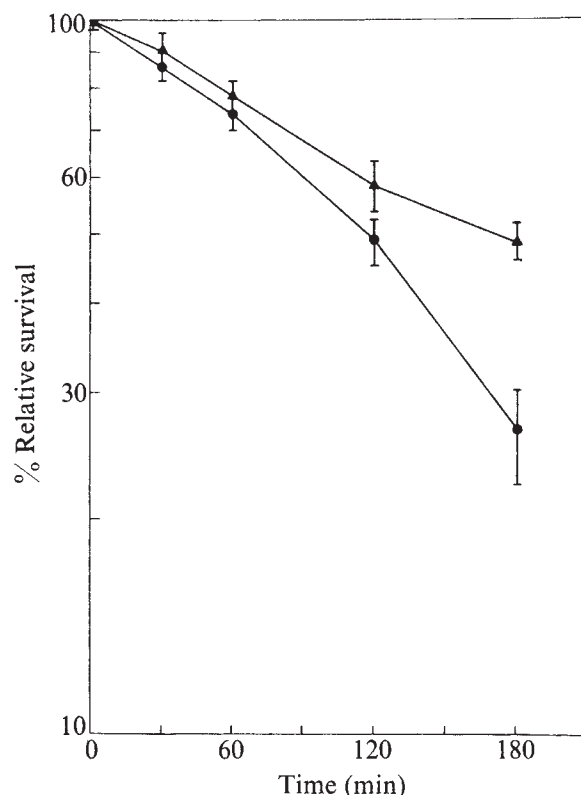


Fig. 1 Toxicity of fluorescent light to V-79 CHL cells incubated in medium or saline. Three hundred exponentially growing V-79 cells were inoculated into 10 ml of CM (α -MEM⁸, minus purines and pyrimidines, containing 5% FCS (Flow Laboratories) and 25 mM HEPES in 100-mm Falcon plastic Petri dishes). The cells were allowed to attach to the dishes at 37 °C in a 7.5% CO₂/air incubator. Four hours after inoculation, some plates were rinsed three times with BSS (without phenol red) containing 25 mM HEPES and incubated at 4 °C in the same solution. Plates containing CM or BSS were placed in a room at 4 °C and irradiated with fluorescent light for the times indicated. All plates were kept in the cold room for 3.5 h. Irradiation was by four Sylvania Cool White F15T8-CW bulbs held in two desk lamps. The bulbs were 8 cm above the surface of the cells and the intensity of illumination at that distance was 1,700 foot candles as measured with a Weston Foot Candle Meter Model 614. Irradiation was from above through both the plastic dish top and the overlying medium. The temperature in the dishes never exceeded 10 °C. After 1 week of incubation, the colonies were rinsed with BSS, fixed in methanol for 10 min, stained with Giemsa and counted. A colony was defined as more than 64 cells in close proximity. The plating efficiency of the unirradiated chilled control cells in CM was 86 $\pm$ 3% (six plates) and in BSS it was 82 $\pm$ 7% (six plates). The number of colonies surviving after light treatment is normalised to the survival of the controls. The mean relative survival $\pm$ % s.d. is plotted. When the standard deviations overlap, the upper and lower limit bars are for the upper and lower points, respectively: $\bullet$, cells irradiated in CM; $\blacktriangle$, cells irradiated in BSS.

These data suggest that the basis of the toxicity of fluorescent light to V-79 cells is primarily a direct action of light on the cells themselves, because toxicity occurs in BSS alone (Fig. 1) and because preirradiated medium does not reduce colony-forming ability (Table 1). Nevertheless, complete medium can potentiate the action of light as shown by the slightly greater killing of cells in medium compared with saline (Fig. 1) and the reduced colony diameter and altered cell morphology caused by pre-irradiated CM (Table 1).

The effect of fluorescent light on the frequency of mutants in V-79 cells is shown in Fig. 2. Resistance to 6-thioguanine was used as a marker for inactive hypoxanthine-guanine phosphoribosyl transferase and as an assay for mutant colonies. The method is described in the legend to Fig. 2. The number of 6-thioguanine-resistant, presumably mutant, colonies increased linearly as the time of exposure to cool white fluorescent light

Table 1 Toxicity of pre-irradiated medium to V-79 Cells

Time of pre-irradiation (h)	% Colony formation relative to controls	Mean colony diameter (mm)	Cellular morphology
0	100 ± 7	0.96 ± 0.38	Normal
1.3	101 ± 5	0.66 ± 0.29	Abnormal
3.0	99 ± 3	0.57 ± 0.36	Abnormal

Three hundred V-79 cells were plated in 100-mm Petri plates as described in the legend to Fig. 1, except that no HEPES was included in the medium. Fifty ml of CM in a closed Corning 150-cm² flask in a room at 4 °C were irradiated with the fluorescent lights described in Fig. 1. To test the effect of irradiating CM on cloning efficiency, the original seeding medium was replaced after 4 h with the same volume of irradiated medium. After 7 d of incubation, colonies were fixed with methanol and stained with Giemsa. The plating efficiency of the controls was 78 ± 3%. The values shown represent the mean survival relative to the controls ± s.d. for three plates. The mean colony diameter and s.d. were determined by measuring 50 colonies on three plates. The differences between the light-treated and untreated means are significant by a *t* test with a *P* value of 0.01. Cellular morphology was examined along the edges of clones with a phase contrast microscope. Morphology was considered abnormal if the cytoplasm was elongated and vacuolated in many clones.

increased (Fig. 2). After 3 h of irradiation in α -MEM the frequency of mutants was 166 times greater than in unirradiated controls. The single point above the line in Fig. 2 shows that after 3 h the frequency of mutants was greater for cells irradiated in BSS than for cells irradiated in CM. This is confirmed by the data in Table 2, which show that fluorescent light was 1.9 times more mutagenic for cells irradiated for 1 h in BSS than for cells irradiated for 1 h in CM.

If 50 ml of CM was used as a filter in a 150-cm² flask placed over the cells in another 150-cm² flask containing 50 ml of BSS, the frequency of mutants was not significantly changed from cells irradiated in CM without a filter (Table 2). This experiment implies that irradiation in CM is less mutagenic

than irradiation in BSS because CM is partially filtering mutagenic portions of the fluorescent lamp emission.

Assuming that a linear dose-response relationship exists for mutagenicity with shorter exposures to light (Fig. 2), it can be calculated from the data presented here that a 1-h exposure to the incident fluorescent light in our tissue culture room (60 foot candles) will double the frequency of mutants in V-79 cells. In most laboratories this amount of exposure or more would occur intermittently on a daily basis. For example, we have found that after killing pre-existing 6-thioguanine-resistant mutants with HAT medium, the frequency of spontaneous mutants will increase progressively during a period of weeks (our unpublished results). This observation might be explained by the mutagenic action of the fluorescent light in our tissue

Table 2 Mutagenicity of fluorescent light for cells irradiated in CM or BSS

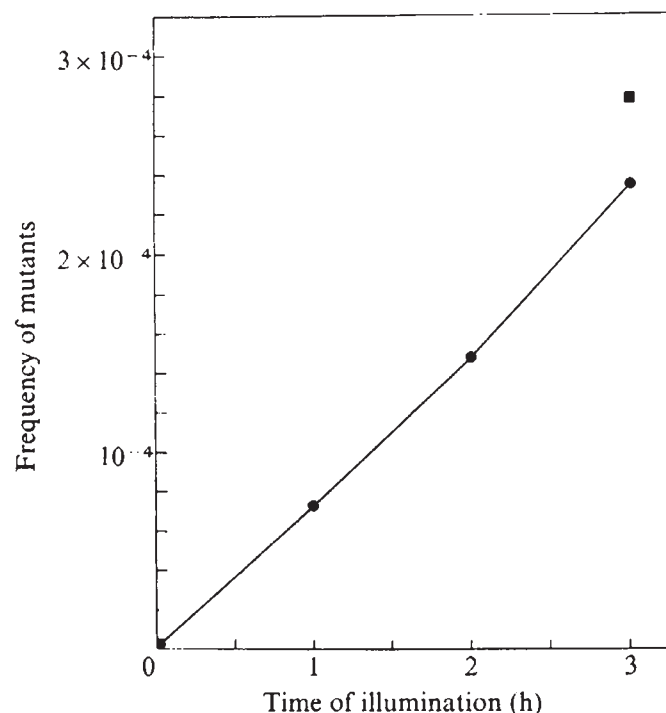
Medium	Filter	Time of irradiation (h)	Frequency of mutants* × 10 ⁻⁶
CM	—	0	1.42 ± 0.21
CM	—	1	38.6 ± 6.4
BSS	—	1	71.9 ± 12.4
BSS	50 ml CM	1	34.1 ± 5.1

The frequency of mutants was determined as described for Fig. 2.

*Mean value ± s.d. of three determinations.

culture hood and culture room that causes the frequency of mutants to increase with each exposure. Therefore it is possible that other genetic instabilities seen in cultured cells, such as malignant and karyotypic alterations, might be accounted for in part by the action of fluorescent light on the cellular DNA.

From the data presented here, we conclude that exposure to fluorescent light should be limited during virtually any study with cultured cells. It is important that all exposure to light in our work was through the plastic tops of the culture vessels. Plastic absorbs more than 99% of any ultraviolet wavelengths less than 295 nm, so that the active wavelengths are presumably



recovered cells among nine 100-mm Petri dishes (3 × 10⁶ cells per dish), in 15 ml of CM containing 6-thioguanine (11 µg ml⁻¹). At the same time, the plating efficiency of these cells was determined by seeding 300 cells each in six 100-mm Petri dishes in CM. Plates were incubated for 1 week before fixing and staining. A colony was defined as containing more than 64 cells. The data for the cultures incubated in CM during exposure to light were analysed statistically using linear regression by the method of least squares. The coefficient of determination for these data is 0.9975; this value is so close to 1.0 that these data can be said to fit a linear equation of the form $y = a_1x + a_0$, where a_1 and a_0 are constants. ■, Culture incubated in BSS during 3 h exposure to light; ●, cultures incubated in CM during 1, 2 or 3 h exposures to light.

Fig. 2 Mutagenicity of fluorescent light to V-79 CHL cells incubated in CM or BSS. The frequency of mutants in V-79 cells after various treatments was measured by a modification of a method described by Myhr and DiPaolo⁸. Briefly, cells were cultured in α -MEM with 5% FCS at 2.5 × 10⁶ cells per 150-cm² Corning plastic flask or per Falcon 15-cm Petri dish. Stock cells were subcultured every Monday and Thursday. On Thursday of each week, 2.5 × 10⁶ stock cells were placed in HAT medium (CM containing 10⁻⁵M hypoxanthine, 3.2 × 10⁻⁶M aminopterin and 5 × 10⁻⁶M thymidine) and subcultured into HAT medium on the next Monday. On the following Thursday, having been in HAT medium for 1 week, cells were trypsinised and incubated in HT medium (CM containing 10⁻⁵M hypoxanthine and 5 × 10⁻⁶M thymidine). On Friday the medium was changed to CM; on Monday HAT-HT-CM cells were inoculated (10⁶ cells each) into 150-cm² flasks in 50 ml of CM. On Wednesday there were usually 3 × 10⁷ cells in log phase in each flask. One flask was trypsinised, and the cells were inoculated into 100-mm Petri dishes to determine the toxicity of the light treatment. The other flasks were irradiated in a room at 4 °C with fluorescent lights as described for Fig. 1. All flasks including controls were pre-incubated at 4 °C for 15 min before irradiation and remained in the cold room for 3.5 h until irradiation was complete. After irradiation the medium was removed and replaced with fresh CM at 37 °C. Two days later cells from the treated and control flasks were subcultured into 150-cm² flasks at 2 × 10⁶ cells per flask to allow further time for mutations to be expressed. The flasks were incubated for at least another 3 d, until cultures were about to become confluent (at about 5–10 × 10⁷ cells) and had undergone at least four population doublings. If the cultures were not approaching confluency within 5 d of treatment, they were incubated until confluency was almost achieved. The fraction of mutant cells in the population at this time was assayed by seeding a total of 2.7 × 10⁶ treated and

longer than 295 nm. Exposure to excessive fluorescent light might produce artefacts in studies of *in vitro* toxicity, mutation, transformation, chromosome variation, ageing, effects of radiation, drug interactions and biochemistry. Whether or not our findings with V-79 Chinese hamster cells will extend to human and other mammalian cells remains to be determined. If human cells are also caused to mutate by fluorescent light, then the advisability of limiting human exposure to fluorescent light should be considered.

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Skin fibroblasts from a D-deletion type retinoblastoma patient are abnormally X-ray sensitive

RETINOBLASTOMA is a rare malignant eye tumour which appears spontaneously or occurs in genetically predisposed persons¹⁻³. The latter group is composed of patients who inherit the tumour with a dominant mode of transmission (80-90% penetrance) (referred to as the familial type) or those who bear a deletion in the long arm of chromosome 13 (13q-) (referred to as the D-deletion type). When this deletion is present, it is observed in many somatic cells and is often associated with structural defects such as microcephaly, microphthalmia and several skeletal and genitourinary abnormalities^{3,4}. Survivors of the genetic forms of retinoblastoma have an increased risk for the development of cancers at other sites, while patients who survive the sporadic type do not²⁻⁶. A single genetic locus is unlikely to predispose many somatic cells to tumour formation unless a fundamental molecular defect—for example, related to DNA repair—is present. To investigate this hypothesis, we have examined the *in vitro* X-ray sensitivity of skin fibroblast strains derived from three retinoblastoma patients—a pair of twins with the familial type accompanied by no gross chromosome abnormalities, and a patient with the D-deletion type. We also used two normal fibroblast strains and a strain from a patient with ataxia telangiectasia. We found that the strain derived from the D-deletion retinoblastoma patient was significantly more radiosensitive than the two normal strains, but not as sensitive as that from the ataxia patient.

Figure 1 shows the X-ray survival curves obtained with skin fibroblasts derived from both a normal individual and a patient with a D-deletion type retinoblastoma³. Also included for comparison is a survival curve for cells from a patient with ataxia telangiectasia; this autosomal recessive disease is associated with marked cellular radiosensitivity *in vitro*⁷, presumably due to an X-ray repair defect⁸. As Fig. 1 shows, the retinoblastoma cells were significantly more sensitive to killing by X rays than were the normal fibroblasts, but not as sensitive as the ataxia cells.

Table 1 presents a comparison of X-ray survival curve parameters for the three retinoblastoma cell strains, two normal

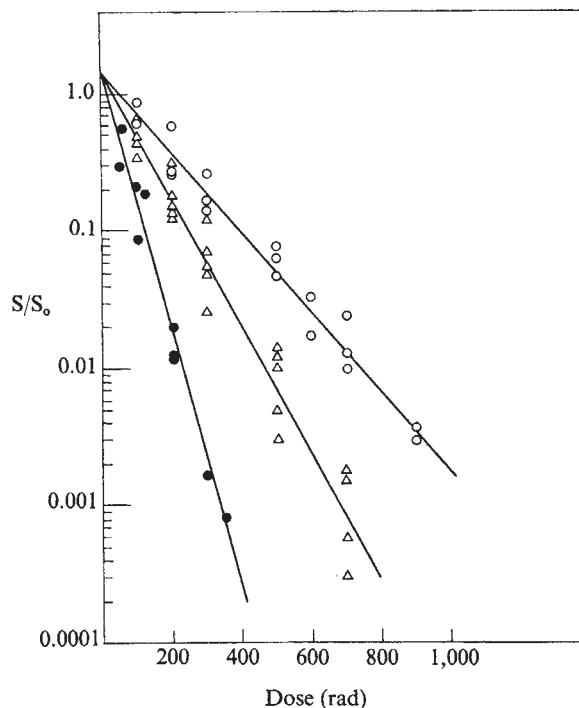


Fig. 1 X-ray survival curves for exponentially growing cultures. Δ , GM1142, skin fibroblasts from a female retinoblastoma patient with a deletion in the long arm of chromosome 13 (46, XX (13q-)); $\bullet$, CRL1343, skin fibroblasts from a patient with ataxia telangiectasia; $\circ$, Li106, normal skin fibroblasts. Cultures were maintained at 37°C in Eagle's minimal essential medium (Gibco F-15) supplemented with 15% foetal calf serum (Flow) D-glucose (900 mg l⁻¹), sodium pyruvate (0.66 mg l⁻¹) and Aureomycin (50 µg ml⁻¹, Lederle) in a 5% CO₂ atmosphere. Cells from each strain were studied at similar passage levels in culture (ranging from 4th to 22nd mean population doubling). For experiments, exponentially growing cells were detached with 0.25% trypsin and seeded at appropriate numbers into 100-mm plastic Petri dishes. Dishes were X-irradiated 18 h later using a 220 kVp GE Maximar unit operated at 15 mA and yielding a dose rate of 80 rad min⁻¹. Dishes were returned to the incubator, the medium was changed after 7 d and the colonies were fixed and stained after 14 d. Cloning efficiencies ranged from 1 to 16%; radiosensitivity was not related to cloning efficiency (Table 1), and previous results have shown no relationship between cloning efficiency and survival curve parameters in several strains of human skin fibroblasts⁹. Points represent the average of triplicate plates. Curves represent a least squares linear regression analysis of the points shown. S/S₀, surviving fraction.

strains and the ataxia strain. The experiments were all performed within 10 weeks using the same lot of serum. Some variations were seen in survival parameters with different serum lots, but the sensitivities of these strains relative to each other remained constant. In nine experiments, including those in Table 1, the D₀ (inverse of the slope) for GM1142 ranged from 70 to 98 rad. The two familial retinoblastoma strains showed radiosensitivities intermediate between the D-deletion retinoblastoma strain and the normal strains, but it is not clear whether these retinoblastoma strains are significantly more radiosensitive than normal controls. As we have found before⁹, the *n* values of the survival curves bore no relationship to radiosensitivity as measured by D₀. We have no explanation for the possible differences in *n* among the cell strains in Table 1. In preliminary experiments, all three retinoblastoma strains appeared normally sensitive to 254 nm ultraviolet irradiation.

As more fibroblast strains from D-deletion retinoblastoma patients become available, it will be interesting to examine their responses to radiation in order to establish whether the radiosensitivity of the retinoblastoma strain described here relates to the fundamental disease process itself or to its

Table 1 X-ray sensitivities of human diploid fibroblast strains

Strain (source)	Clinical classification	Age/sex of donor	No. of experiments	Cloning efficiency	n^*	$D_{0.5}^*$
GM1142 (IMR)	Retinoblastoma D-deletion type	2 yr/F	6	0.7–6.5%	1.41 ± 0.3	94 ± 5
GM1131 (IMR)	Retinoblastoma familial type	9 mon/F	3	3.0–16.5%	0.87 ± 0.09	132 ± 4
GM1123 (IMR)	Retinoblastoma familial type (twin of GM1131)	9 mon/F	3	1.2–12.4%	1.03 ± 0.1	121 ± 4
CRL1343 (ATCC)	Ataxia telangiectasia	7 yr/F	3	0.7–1.8%	1.39 ± 0.4	46 ± 3
GM1381 (IMR)	Normal infant	2 mon/F	3	0.6–1.7%	0.99 ± 0.1	148 ± 9
Li106 (primary culture)	Normal adult	46 yr/M	6	1.0–6.3%	1.44 ± 0.2	149 ± 7

The data were obtained as described for Fig. 1.

IMR, Institute for Medical Research, Camden, New Jersey; ATCC, American Type Culture Collection, Rockville, Maryland; $D_{0.5}$, inverse of slope; n , extrapolation number to vertical axis.

*Mean $\pm$ 1 s.e. from least squares linear regression analysis of all data.

association with an abnormal karyotype involving a specific chromosomal region and perhaps a specific gene product. Patients with familial retinoblastoma may bear a much smaller deletion not detectable by available karyotypic and banding methods.

It is tempting to speculate that a specific X-ray repair function is governed by a portion of chromosome 13. Thus the predisposition to cancer in these patients might be related to a fundamental defect in a particular DNA repair system, analogous to the relationship between a deficiency in ultraviolet light repair and the predisposition to skin tumours in patients with xeroderma pigmentosum¹⁰.

We conclude that skin fibroblasts derived from a patient with the D-deletion variant of retinoblastoma are abnormally radiosensitive. Perhaps future investigations will delineate a specific defect in molecular repair of DNA that will explain the predisposition of these patients to develop second primary tumours.

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Inhibition by sera and soluble antigens of T-cell-mediated cytotoxicity against leukaemia-associated antigens

INTEREST in the regulation of T-cell-mediated cytotoxicity by the major histocompatibility complex (MHC) genes stems from the discovery of (1) an H-2 restriction of T-cell-mediated cytotoxicity, that is sensitising cells, effector cells and target cells need to be syngeneic at the H-2 locus, especially at the D and or K regions of the MHC^{1–5} for effective killing and (2) inhibition of T-cell-mediated cytotoxic reactions against syngeneic tumours with

alloantibodies to H-2 antigens specific for the tumour cells^{6,7}. Different origins have been proposed for the tumour-associated antigens (TAA), and the most favourable model is a modified H-2 antigen or an adaptor-antigen complex^{4–7}. This issue has important implications for tumour immunology, and so we have evaluated the validity of the inhibition of cytotoxicity by serum at the effector phase level; investigated afferent interference by serum of the cell-mediated cytotoxic response, and studied the inhibition of cell-mediated cytotoxic reactions with soluble antigens. We report here that there is a lack of H-2 restriction of T-cell-mediated cytotoxicity to TAA, and that TAA seems to differ from H-2 antigens. This implies that T-cell recognition is not entirely regulated by the MHC genes.

A 20-h ¹²⁵IUDR release assay (IRA) (ref. 8) was used to measure cell-mediated cytotoxic response to FBL-3 (ref. 9), a syngeneic Friend virus-induced lymphocytic leukaemia in C57BL/6 (B6) mice. The cytotoxic reactions were found to be primarily directed against the Friend Moloney-Rauscher (FMR) leukaemia-associated antigens^{10–12}. Both the induction phase and the effector phase of these cytotoxic reactions were entirely T-cell-dependent. Pretreatment of the responding cells¹⁰ or the effector cells^{11,12} with anti- θ antibody plus complement eliminated cytotoxicity. Furthermore, removal of adherent cells and macrophages by passage of the effector cells through a rayon column or incubation in a Petri dish did not affect the level of cytotoxicity^{11,12}. Thus the reactions were apparently not macrophage-mediated. When various antisera and normal sera were used to study their effects on these cytotoxic reactions (Table 1), we found that effector cells which were generated in B6 mice (H-2^b) by immunisation with syngeneic FBL-3 cells killed both the syngeneic target FBL-3 and an allogeneic target HFL/d-tc, a non-producer line of Friend virus-induced leukaemia in BALB/c (H-2^d) mice¹³. In other experiments, effective killing of FBL-3 and HFL/d-tc cells could also be achieved by lymphocytes obtained in BALB/c mice which were immunised with syngeneic HFL/d-tc cells¹⁴. These lymphocytes gave even higher levels of cytotoxicity against the allogeneic target FBL-3 than against the syngeneic target HFL/d-tc. In our experiment, an alloantisera with the appropriate specificity, and the syngeneic serum produced against FBL-3 both inhibited cytotoxicity. In addition normal mouse serum (NMS) gave inhibition against FBL-3 targets.

If NMS or normal rabbit serum were used as a baseline for calculations of cytotoxicity, various other sera, for example, anti-FBS, which bound to the foetal bovine serum coated on the surface of target cells and rabbit anti-mouse cell serum, also inhibited the reactions against both FBL-3 and HFL/d-tc. Anti-Ia, and rabbit anti-mouse Ig, inhibited the reaction against FBL-3. None of the last four sera in Table 1 should contain antibody against H-2 antigens. Thus, it seems that any antibodies that bind to the cell surface can interfere with the cytotoxic reactions, perhaps by steric hindrance. This conclusion was also suggested by the following results. (1) Pretreatment of either the target cells or effector cells

Table 1 Inhibition of cell-mediated cytotoxic reactions with sera

Serum	Target cells					
	FBL-3			HFL/d-tc		
	Net % lysis	Net % lysis(s)	<i>P</i>	Net % lysis	Net % lysis(s)	<i>P</i>
None	49			18		
NMS	32			15		
Anti-H-2 ^b	4	-28	< 0.01	17	2	
Anti-H-2 ^d	47	15		10	-5	< 0.01
Anti-FBL-3	19	-13	< 0.01	10	-5	< 0.01
Anti-FBS	14	-18	< 0.01	7	-7	< 0.01
Anti-Ia	27	-5	< 0.05	ND		
NRS	46			18		
RAM	-5	-51	< 0.01	8	-10	< 0.01
RAG	10	-36	< 0.01	23	5	

¹²⁵IUDR release assay was performed in Microtest II plates. E/T (ratio of effector : target cells) = 500/1, incubation time was 20 h. Effector cells were the pooled lymph node and spleen cells obtained from B6 mice immunised by subcutaneous inoculation of 5×10^6 FBL-3 cells 10 d before assay. Various sera were added to the test wells at final dilutions of 1/5. NMS, normal mouse serum. Anti-H-2^b was from BALB/c immunised with B6 skin grafts and spleen cells. Anti-H-2^d was from B6 immunised with BALB/c skin graft and spleen cells. Anti-FBL-3, B6 immunised with FBL-3. Anti-FBS, B6 immunised with foetal bovine serum. Anti-Ia was from (B10.A × F); immunised with B6 spleen, absorbed with B6 tumour EL-4 cells (given by Dr David Sachs, NIH). NRS, normal rabbit serum. RAM was from rabbit immunised with mouse tumour (SV40 tumour mKSA in BALB/c). RAG, rabbit anti-mouse Ig. Net % lysis = (total % lysis obtained with immune lymphocytes) - (total % lysis obtained with normal lymphocytes). Net % lysis(s) = (net % lysis obtained with immune lymphocytes plus antiserum) - (net % lysis obtained with immune lymphocytes plus normal serum). Welch distribution *t* test was used to determine statistical significance. The results were compared to net percentage of lysis obtained with immune lymphocytes plus normal serum (NMS or NRS).

with antisera for up to 4 h followed by a single wash did not reduce cytotoxicity (data not shown); whereas significant antibody binding to the FBL-3 cells could still be demonstrated after five washes (Fig. 1). This indicates that excess antiserum is needed for inhibition. (2) The degree of inhibition by the serum was in approximate proportion to the amount of the antibody bound to the cell surface (Fig. 1). The isotopic antiglobulin technique (IAT)¹⁵, which measures the amount of antibody bound to the cell surface indicated that the four mouse sera tested gave relative binding to FBL-3 cells in the order anti-H-2^b > anti-FBS > anti-FBL-3 > anti-Ia. When these sera were used in the IRA to assay

for their ability to inhibit the cytotoxicity against FBL-3, the same order of effectiveness was found, that is anti-H-2^b was most inhibitory, and anti-Ia was least inhibitory. The anti-H-2^d serum which did not bind to FBL-3 cells also gave no inhibition of cytotoxicity. These results suggest that inhibition by serum need not depend on binding to specific structures, but only on binding to the cell surface, and they are consistent with inhibition being due to non-specific steric hindrance. The effective inhibition of the cytotoxic reaction obtained with rabbit anti-mouse Ig serum supports this possibility although it is not clear why this serum binds to the target cells. In addition, the inhibition of the killing of H-2^d target (HFL/d-tc) by anti-H-2^d seems to be non-specific, because the killer cells were generated by syngeneic immunisation with FBL-3 (H-2^b) and therefore presumably are not directed against any H-2^d-associated antigens.

We have shown that specific afferent interference of transplantation immunity to FBL-3 could be produced by pretreatment of the immunising cells with specific anti-tumour antiserum¹⁶. It follows that if TAA is truly modified H-2, then anti-H-2 antibody should produce similar interference. Therefore various sera were used to determine their effect on the induction of cell-mediated cytotoxic response to FBL-3 in the syngeneic B6 host (Table 2). Only pretreatment with syngeneic anti-FBL-3 serum could specifically reduce the cytotoxic response. Neither anti-H-2^b, nor anti-FBS had any effect, providing further evidence that TAA is not associated with H-2 antigen.

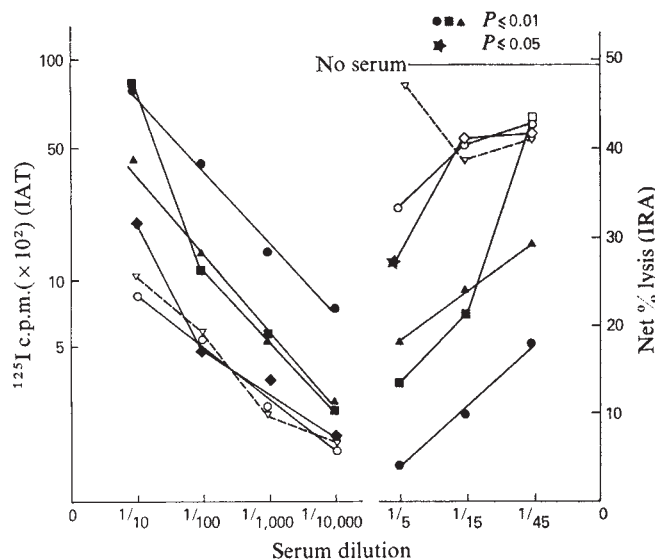


Fig. 1 Reaction of various sera to FBL-3 cells in the isotopic antiglobulin technique (IAT), and their effects on the cell-mediated cytotoxic reaction in the ¹²⁵IUDR release assay (IRA). In IAT, 0.1-ml samples of sera at various dilutions were incubated with 1×10^5 FBL-3 cells, then washed five times, followed by incubation with ¹²⁵I-labelled goat anti-mouse Ig. They were washed five times, and the radioactivity of the cell pellets were counted in a γ scintillation counter. The relative amounts of antibody bound to the cell surface were indicated as ¹²⁵I c.p.m. and were relative to that of normal mouse serum (NMS). In IRA, effector cells were obtained from B6 mice immunised with syngeneic tumour FBL-3 and tested against FBL-3 in Microtest II plates with E/T = 500/1 and incubation for 20 h. In this experiment, 0.1-ml samples of sera at various dilutions were added to the test wells to determine their effects on the inhibition of cytotoxicity. The statistics were evaluated by the Welch distribution *t* test. The results were compared to net percentage of lysis obtained with effector cells with addition of NMS. The mouse sera were the same as for Table 1. ∇ , Anti H-2^d; $\circ$, NMS; $\star$, $\blacklozenge$, anti-Ia; $\blacktriangle$, anti-FBL-3; $\blacksquare$, anti-FBS; $\bullet$, anti-H-2^b.

Table 2 Afferent interference of cell-mediated cytotoxic response with sera

Pretreatment*	Net % lysis obtained at E/T	
	200/1	40/1
Exp. 1		
None	26	3
NMS	28	5
Anti-FBL-3	14†	1
Anti-H-2 ^b	29	3
Anti-FBS	24	5
Exp. 2		
None	51	23
NMS	45	22
Anti-FBL-3	11†	2†
Anti-H-2 ^b	43	20
Anti-FBS	46	23

* 1×10^5 of 10,000-R X-irradiated FBL-3 cells were incubated with 0.5 ml of undiluted serum at 37 °C for 60 min. Then 1×10^4 untreated or serum-treated cells were inoculated intraperitoneally into B6 mice. ¹²⁵IUDR assay was performed with peritoneal exudate cells 7 d after immunisation.

† *P* < 0.01; statistical significance was evaluated by the Welch distribution *t* test. The results were compared to net percentage of lysis obtained from mice immunised with untreated cells or normal serum-treated cells.

Finally, three different soluble antigens were tested for their effects on the cell-mediated cytotoxic reactions to FBL-3: papain-solubilised FBL-3 membrane antigen, papain-solubilised H-2^b antigen obtained from dissociated B6 spleen cells, and purified viral protein, gp70, prepared from Rauscher virus (given by Dr S. Oroszlan, Flow). The results are summarised in Table 3. Soluble FBL-3 antigen at concentrations as low as 7.5 $\mu\text{g ml}^{-1}$ gave complete inhibition of the cytotoxicity; no inhibition could be obtained with H-2^b antigen even at 50 $\mu\text{g ml}^{-1}$. The purified gp70 gave 20–30% inhibition at 2.5–12.5 $\mu\text{g ml}^{-1}$. A mixture of gp70 and H-2^b antigen produced the same inhibition as gp70 alone. These data indicate that unaltered H-2^b antigenic specificities are not present on the receptor site recognised by these cytotoxic lymphocytes although modified H-2^b is not excluded as a target. The viral antigen gp70 is a cytotoxic target, but the fact that partially purified H-2^b does not enhance its inhibitory activity suggests that H-2^b-gp70 complexes are not usually targets, although such a complex might not be obtained easily in a cell-free system. The observation that the soluble FBL-3 preparation can totally inhibit cytotoxicity argues against the existence of H-2-tumour antigen complexes since this material is prepared by papain digestion and such non-covalent complexes would be unlikely to survive such harsh treatment.

Table 3 Inhibition of cell-mediated cytotoxic reactions with soluble antigens

Antigens	Concentration* ($\mu\text{g ml}^{-1}$)	Net % lysis	% Reduction†
None		61	
FBL-3	25.0	–2	103
FBL-3	7.5	5	92
FBL-3	2.5	35	43
H-2 ^b ‡	50.0	62	–1
H-2 ^b ‡	10.0	62	–2
gp70	12.5	43	30
gp70	2.5	48	22
H-2 ^b + gp70	(50 + 12.5)	49	21
H-2 ^b + gp70	(10 + 2.5)	50	19

¹²⁵IUdR assay was performed as for Table 1.

*Final concentration of soluble antigen in test wells.

†% of reduction = (net % lysis obtained with immune lymphocytes alone) – (net % lysis obtained with immune lymphocytes plus soluble antigen).

net % lysis obtained with immune lymphocytes alone

‡H-2^b was solubilised with papain and purified 200-fold from B6 spleen cells (M.J.R., unpublished data). When labelled, 40% of the preparation can be specifically precipitated with anti-H-2^b alloantisera.

We have demonstrated that efficient killing of allogeneic targets by T lymphocytes is generated by syngeneic immunisation (Table 1); that efferent inhibition of cytotoxicity by alloantisera can be non-specific (Fig. 1); that specific afferent inhibition of the cytotoxic response is only provided by syngeneic anti-tumour serum, not alloantisera (Table 2); that complete inhibition of cytotoxic reactions can only be obtained with soluble tumour antigen, not H-2 antigen (Table 3) and that cytotoxicity against syngeneic targets can be generated by allogeneic immunisation^{14,17}.

These data strongly suggest that there is no H-2 restriction of T-cell-mediated cytotoxicity to specific leukaemia-associated antigen(s) in this system. The findings are also contrary to the hypothesis of the TAA measured by our cytotoxicity assay being an (H-2) adaptor-(tumour) antigen complex. The discrepancy between these results and other reports of H-2 restriction could be due to differences in the assays. We have found that a 4–10 h ⁵¹Cr release assay which was used by others^{1–7}, fails to detect the killing of allogeneic targets which may require longer incubation (20–40 h) (ref. 14). The explanation for this discrepancy is that MHC genes can play some role in the initial recognition phase of the cytotoxic reaction, thus enhancing short term killing in syngeneic target effector combination. The MHC genes are not essential, however, because recognition of specific, non-MHC antigens by allogeneic effector cells can produce effective cytotoxicity which becomes evident with longer incubation time.

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Active site of bovine factor XI (plasma thromboplastin antecedent)

FACTOR XI (plasma thromboplastin antecedent) is a plasma glycoprotein which participates in the early stages of blood coagulation¹. A deficiency of this protein leads to a haemorrhagic disease in which the intrinsic pathway of blood coagulation is partially or completely blocked². During normal coagulation, factor XI is converted to a serine protease (factor XI_a)³, and this enzyme in turn activates factor IX (Christmas factor) by limited proteolysis⁴. Factor XI_a is inhibited by serine protease inhibitors such as diisopropyl phosphorofluoridate, and this inhibitor is bound to a serine residue in the active site of the enzyme⁵. We recently purified bovine factor XI approximately 28,000-fold in 30% yield. The final preparation was

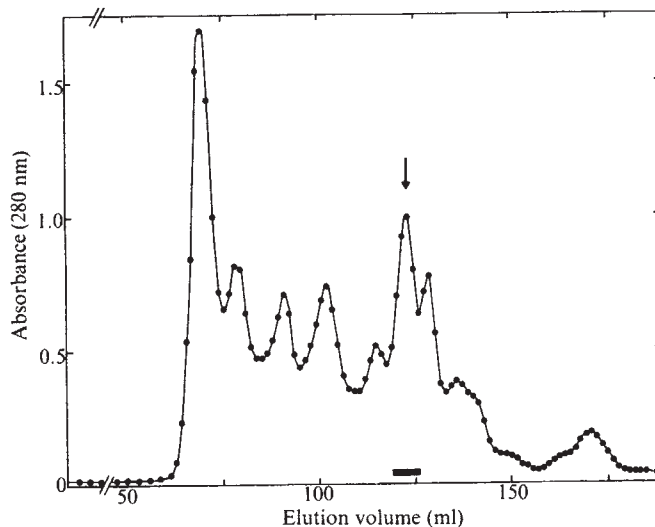


Fig. 1 Gel filtration pattern of the cyanogen bromide digest of S-pyridylethyl bovine factor XI. Factor XI, 40 mg, was pyridylethylated by the method of Friedman *et al.*¹⁵ and the protein was separated from the salt and excess reagent by gel filtration on Sephadex G-50 (1.8 cm $\times$ 50 cm column) in the presence of 9% formic acid. Cyanogen bromide digestion was carried out by dissolving 40 mg of the salt-free S-pyridylethyl factor XI and 80 mg of cyanogen bromide in 2 ml of 70% formic acid, and the reaction was allowed to proceed for 24 h at 4 °C. After lyophilisation, the digest was fractionated by gel filtration on Sephadex G-75 (1.6 cm $\times$ 90 cm column) in the presence of 9% formic acid. The flow rate was 4.2 ml h⁻¹ and fractions were collected in 1.4 ml per tube. The solid bar shows the fractions of peak 6 that were combined and lyophilised.

		180		185		190		195	
Factor XI	Val	Cys Ala Gly Tyr	Arg	-	Glu Gly Gly Lys	-	-	Asp Ala Cys Lys	Gly Asp SER Gly Gly Pro
Factor XII*	Leu	Cys Ala Gly	Phe Leu	-	Glu Gly Gly Thr	-	-	Asp Ala Cys Gln Gly Asp SER Gly Gly Pro	
Factor IX _a †	Phe	Cys Ala Gly Tyr	His	-	Glu Gly Gly Lys	-	-	Asp Ser Cys Gln Gly Asp SER Gly Gly Pro	
Factor X _a ‡	Phe	Cys Ala Gly Tyr	Asp	-	Thr Gln Pro Glu	-	-	Asp Ala Cys Gln Gly Asp SER Gly Gly Pro	
Thrombin§	Phe	Cys Ala Gly Tyr	Lys Pro Gly Glu	Gly Lys	Arg Gly	Asp Ala Cys	Glu	Gly Asp SER Gly Gly Pro	

Fig. 2 Active site sequence of bovine factor XI and several other blood coagulation proteins. Amino-terminal sequence analysis was performed on 1.2-mg samples of peak 6, Fig. 1, with a Beckman sequencer Model 890A. The operation of this instrument and the methods used are adaptations¹⁶ of Edman and Begg's technique¹⁷. Phenylthiohydantoin amino acids were identified by gas chromatography after silylation or directly by high-pressure liquid chromatography¹⁸. Amino acid residues in factor XI that are identical with other plasma serine proteases are shown in blocks. —, spaces inserted to bring the five proteins into alignment for better homology. The numbering system is that of chymotrypsin where the active site serine is residue 195. * Ref. 19; † ref. 20; ‡ ref. 21; § ref. 22.

homogeneous as measured by sodium dodecyl sulphate polyacrylamide gel electrophoresis and immunoelectrophoresis⁶. It has a molecular weight of 124,000 as determined by sedimentation equilibrium and is composed of two similar or identical polypeptide chains held together by a disulphide bond(s). We present here data showing that bovine factor XI contains an amino acid sequence which is very similar to the active site region of many other serine proteases involved in the coagulation process.

S-pyridylethyl factor XI was digested with cyanogen bromide and the polypeptide fragments were fractionated by gel filtration on Sephadex G-75 (Fig. 1). Twelve ultraviolet-absorbing peaks were obtained. Peak 6 (shown by the arrow) migrated as a single band on sodium dodecyl sulphate polyacrylamide gel electrophoresis and had a molecular weight of approximately 5,500. The amino-terminal sequence of this polypeptide chain is shown in Fig. 2, with the active site regions of several other coagulation proteins from bovine plasma. Twenty residues were identified in this peptide. The amino-terminal residue was valine and no other amino acids were detected. The active site serine, corresponding to serine 195 in chymotrypsin, appeared in position 17 of the peptide. The yield of this residue, however, was poor. For the remaining amino acids, the repetitive yields for the degradations were about 95% and over 80% of the expected quantities of the phenylthiohydantoin based on the weight of the lyophilised peptide. It is clear from these data that bovine factor XI contains an amino acid sequence which is characteristic of the active site regions of a number of plasma serine proteases. This sequence is also homologous to that found in pancreatic trypsin⁶ and is consistent with the fact that factor XI_a has esterase activity towards benzoylarginyl ethyl ester³ and participates in blood coagulation by splitting an arginyl valyl peptide bond in factor IX (P. Lindquist, K. Fujikawa and E. W. Davie, in preparation). A specificity toward basic amino acids is also consistent with the fact that residue 189 in factor XI is aspartic acid. This residue is in the bottom of the binding pocket in trypsin and forms an ion pair with an arginine or lysine residue in the substrate⁷⁻¹².

Bovine factor XI, like factor XII (Hageman factor), factor IX_a, factor X_a (activated Stuart factor) and thrombin, also contains an aspartic acid residue in position 194 next to serine 195. When trypsinogen and chymotrypsinogen are converted to enzymes, aspartic acid 194 forms an ion pair with the newly formed α-amino group of isoleucine which is generated during the activation reaction^{13,14}. It seems likely that a similar mechanism may occur when factor XI is converted to a serine protease by limited proteolysis.

Factor XI contains 12 methionine residues per 124,000 g of glycoprotein⁵. This should yield 14 cyanogen bromide peptides for a molecule composed of two non-identical chains, or seven peptides for a molecule composed of two identical chains. Approximately 12 cyanogen bromide fractions were detected by gel filtration on Sephadex G-75 (Fig. 1). Examination of each of these peaks by sodium dodecyl sulphate polyacrylamide gel electrophoresis indicated, however, that many of these peaks

were not homogeneous. Thus, the question as to whether factor XI is composed of two identical chains or two very similar chains remains to be answered.

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Depression: a new animal model sensitive to antidepressant treatments

A MAJOR problem in the search for new antidepressant drugs is the lack of animal models which both resemble depressive illness and are selectively sensitive to clinically effective antidepressant treatments. We have been working on a new behavioural model in the rat which attempts to meet these two requirements. The method is based on the observation that a rat, when forced to swim in a situation from which there is no escape, will, after an initial period of vigorous activity, eventually cease to move altogether making only those movements necessary to keep its head above water. We think that this characteristic and readily identifiable behavioural immobility indicates a state of despair in which the rat has learned that escape

Table 1 Effects of various psychotropic drugs on the total duration of immobility induced in rats forced to swim in a narrow cylinder for 5 min

Experimental treatment	Dose (mg kg ⁻¹ i.p.)	No. of rats per group	Duration of immobility (s) (mean $\pm$ s.e.)	P (difference from control)
Tricyclic antidepressants				
Imipramine HCl	Control	5	224.4 $\pm$ 4.7	—
	7.5	5	188.2 $\pm$ 14.6	N.S.
	15	5	138.0 $\pm$ 14.5	< 0.01
	30	5	132.4 $\pm$ 25.9	< 0.01
Desimipramine HCl	Control	5	214.2 $\pm$ 8.2	—
	2.5	5	220.8 $\pm$ 22.8	NS
	5	5	202.2 $\pm$ 14.3	NS
	10	5	174.8 $\pm$ 16.8	NS
	20	5	98.8 $\pm$ 17.6	< 0.01
Amitriptyline HCl	Control	10	245.4 $\pm$ 8.0	—
	3.75	5	184.4 $\pm$ 5.5	< 0.05
	7.5	10	189.7 $\pm$ 18.9	< 0.05
	15.0	10	150.7 $\pm$ 22.2	< 0.01
Monoamine oxidase inhibitor				
Nialamide HCl	Control	10	224.1 $\pm$ 9.6	—
	40	10	231.2 $\pm$ 20.3	NS
	80	5	127.4 $\pm$ 29.6	NS
	100	5	83.4 $\pm$ 43.0	< 0.01
ECS	Control	10	238.7 $\pm$ 13.2	—
	ECS	10	166.0 $\pm$ 24.7	< 0.05
Atypical antidepressants				
Iprindole HCl	Control	10	243.1 $\pm$ 14.1	—
	7.5	5	268.4 $\pm$ 11.1	NS
	15	5	237.8 $\pm$ 15.9	NS
	30	5	229.4 $\pm$ 21.3	NS
	40	5	155.6 $\pm$ 24.8	< 0.01
	60	5	260.6 $\pm$ 15.8	NS
Mianserin HCl	Control	5	210.6 $\pm$ 21.1	—
	3.75	5	187.2 $\pm$ 8.9	NS
	7.5	5	187.6 $\pm$ 11.2	NS
	15	5	140.0 $\pm$ 14.7	< 0.01
	30	5	147.2 $\pm$ 11.5	< 0.05
	60	5	256.4 $\pm$ 16.6	NS
Viloxazine HCl	Control	10	214.8 $\pm$ 12.1	—
	7.5	5	207.6 $\pm$ 30.2	NS
	12.5	5	205.6 $\pm$ 12.9	NS
	15	5	202.6 $\pm$ 21.1	NS
	25	5	176.0 $\pm$ 23.2	NS
	30	5	171.0 $\pm$ 15.1	NS
	50	5	144.8 $\pm$ 15.3	< 0.05
Psychostimulants				
(+)Amphetamine sulphate	Control	5	202.8 $\pm$ 17.9	—
	0.75	5	175.0 $\pm$ 9.2	NS
	1.5	5	85.4 $\pm$ 19.4	< 0.01
	3.0	5	25.4 $\pm$ 23.2	< 0.01
Caffeine	Control	5	219.6 $\pm$ 20.7	—
	3.75	5	257.4 $\pm$ 8.7	NS
	7.5	5	177.2 $\pm$ 21.7	NS
	15	5	99.8 $\pm$ 21.0	< 0.01
Anxiolytics				
Chlordiazepoxide HCl	Control	5	237.6 $\pm$ 8.9	—
	2	5	237.2 $\pm$ 16.0	NS
	4	5	225.6 $\pm$ 9.6	NS
	8	5	234.6 $\pm$ 9.4	NS
Diazepam	Control	5	208.0 $\pm$ 10.7	—
	0.5	5	224.6 $\pm$ 10.7	NS
	1	5	242.6 $\pm$ 12.7	NS
	2	5	216.6 $\pm$ 19.8	NS
	4	5	222.2 $\pm$ 21.1	NS
Major tranquillisers				
Chlorpromazine HCl	Control	5	218.2 $\pm$ 2.2	—
	0.75	5	220.6 $\pm$ 11.8	NS
	1.5	5	224.0 $\pm$ 18.1	NS
	3	5	263.0 $\pm$ 8.2	< 0.05
Ro4-1284	Control	5	202.6 $\pm$ 7.3	—
	1	5	271.2 $\pm$ 12.6	< 0.01
	2	5	271.0 $\pm$ 12.0	< 0.01
	4	5	257.8 $\pm$ 15.9	< 0.01

The rats had previously received three intraperitoneal injections 24, 5 and 1 h before testing. The doses, expressed in terms of the salt, are those given at each injection. The drugs were dissolved or suspended in 0.9% NaCl and injected in a constant volume of 5 ml kg⁻¹. Differences from control values were assessed for statistical significance using the Dunnett test (two-tailed)¹⁵.

is impossible and resigns itself to the experimental conditions. This hypothesis receives support from results presented below which indicate that immobility is reduced by different treatments known to be therapeutic in depression including three drugs, iprindole, mianserin and viloxazine which although clinically active¹⁻³ show little or no 'antidepressant' activity in the usual animal tests⁴⁻⁶.

Naive male Sprague-Dawley (Charles River) rats weighing between 160 and 180 g are plunged individually into a vertical plexiglass cylinder (height 40 cm; diameter 18 cm) containing 15 cm of water maintained at 25 °C. After 15 min in the cylinder they are removed and allowed to dry for 15 min in a heated enclosure (32 °C) before being returned to their individual cages. This treatment produces long periods of immobility in the water (10-12 min total duration) and the rats on removal are mildly hypothermic (-3 °C) and are hypoactive for periods up to 30 min. 24 h later the rats are replaced in the cylinder and the total duration of immobility is measured during a 5-min test. Rats submitted to this procedure will remain immobile for 75% of the duration of the test (see Table 1) thus providing a suitable baseline for measuring the effects of drugs which decrease or even increase immobility.

Drugs and doses investigated are shown in Table 1. To optimise the pharmacological effect⁷ and at the same time to imitate more closely clinical usage, we administered the drugs in a series of three intraperitoneal injections 24, 5 and 1 h before testing on day 2, the first injection being given immediately before replacing the animals in their cages on day 1. Electroconvulsive shock (ECS; 30 mA, 50 Hz, 1 s) was delivered through ear-clip electrodes according to the same time schedule as for drug injections.

Table 1 shows that all the antidepressants tested as well as ECS significantly reduced immobility. With the tricyclic compounds, particularly amitriptyline, this 'antidepressive' effect was accompanied by lowered muscle tonus and diminished motor activity outside the test situation suggesting sedation. Biphasic effects were observed with mianserin and iprindole: a reduction in immobility at lower doses followed at higher doses by a return to control levels and a marked loss of muscle tonus. Viloxazine decreased immobility without apparent sedative effects. The monoamine oxidase inhibitor, nialamide, reduced immobility but induced small repetitive body movements which were not observed with the tricyclic antidepressants; loss of muscle tonus was noted at 100 mg kg⁻¹. The two psychostimulants (+)-amphetamine and caffeine also reduced immobility but in contrast to the tricyclic compounds induced a marked hyperactivity; with (+)-amphetamine stereotyped head movements were observed at 1.5 and 3 mg kg⁻¹. Neither chlorthalidoxepoxide nor diazepam affected the duration of immobility even at doses which produced noticeable ataxia. In contrast, both chlorpromazine and the reserpine-like compound RO4-1284 increased mobility; with RO4-1284 a ceiling effect was already observed at 1 mg kg⁻¹, a non-cataleptic dose.

We conclude from the results obtained that the immobility induced in these experiments reflects a state of lowered mood in the rat. Immobility was reduced by antidepressant drugs and ECS, was unaffected by anxiolytics, and was increased by drugs known to be capable of inducing depressive states in man^{8,9}. The positive findings obtained with amphetamine and caffeine do not stand in contradiction to this conclusion as both compounds do possess some clinical antidepressant activity¹⁰ and besides, the effects observed could be distinguished qualitatively from those of the non-stimulant antidepressants.

The results obtained with mianserin deserve comment because this compound, although clinically active², possesses a profile of pharmacological and biochemical activity which is almost the mirror image of that expected

of a classical tricyclic antidepressant: it potentiates the effects of reserpine and antagonises the effects of amphetamine¹¹. It does not inhibit the re-uptake of monoamines¹² and is moreover a potent blocker of central 5-hydroxytryptamine receptors¹³. Although providing no explanation for the mechanisms of action of mianserin, it is noteworthy that the present procedure, which is based on behavioural rather than biochemical concepts, is the first animal test model which would predict an antidepressant action for this compound. Furthermore the bimodal effect observed strikingly parallels clinical observations showing an optimal antidepressant effect at intermediate doses¹⁴.

These positive findings, together with those obtained with the two other atypical compounds, iprindole and viloxazine, raise the intriguing possibility that the method described here might be capable of discovering new types of antidepressant agents hitherto undetectable using classical screening tests.

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Benzodiazepine receptors in rat brain

HIGH affinity binding of tritium labelled morphine and morphine-like drugs to membranes in brain homogenates¹⁻³ was a decisive advance in the characterisation of opiate receptors and the discovery of enkephalines and endorphines. We report here experiments which suggest that another important group of psychoactive drugs, the benzodiazepines, bind to specific receptors on the membranes of rat brain cells. This suggests that there may be an unknown endogenous neurotransmitter which is the natural ligand for the benzodiazepine receptor. The binding sites are distributed unevenly through the brain, and displacement potencies of benzodiazepines correlate with pharmacological effects predictive of anxiolytic activity.

Whole forebrains (excluding cerebellum and pons-medulla) of 150 g Wistar rats were homogenised gently in 20 volumes of ice-cold 0.32 M sucrose, centrifuged at 1,000g for 10 min and recentrifuged at 30,000g to give a crude P₂-synaptosomal fraction. The P₂-fraction was rehomogenised in an equal volume of hypotonic, 50 mM, Tris-HCl (pH 7.5). The binding assay consisted of 500 µl test drug solution and with ³H-diazepam as the radioactive ligand, usually at 1.6 nM (³H-diazepam (*N*-methyl-³H) 14, 4 Ci mmol⁻¹; provided by Dr Willy Haefely, Hoffmann-La Roche). The mixture was preincubated for 5 min at 37 °C before addition of ³H-diazepam followed by a 15 min additional incubation. The

samples were cooled for 30 min in an ice bath and membranes with bound ^3H -diazepam were isolated on Whatman GF/C glassfibre filters. At the end of the incubation 10 ml of iced buffer (50 mM Tris-HCl, pH 7.4) was added, immediately before filtering, and the filter was washed with an additional 10 ml iced buffer and bound diazepam was estimated by conventional scintillation counting.

The amount of nonspecific binding, defined as binding in the presence of excess unlabelled ligand, was very low. Addition of diazepam at $3\text{ }\mu\text{M}$ to the binding assays displaced 91–93% of the total ^3H -diazepam binding. Specific ^3H -diazepam binding was saturable (Fig. 1) and maximal binding was obtained with about 50 nM ^3H -diazepam. A Scatchard analysis of the results in Fig. 1 yielded a single straight line in the concentration range below 50 nM , indicating the presence of a single binding site. The affinity constant, K_D (concentration of ^3H -diazepam giving half-maximal binding) was 2.6 nM and the total number of binding sites was 18 pmol per g original tissue. Hill plots (not shown) had a slope of $1.0\text{--}1.1$ indicating absence of cooperativity.

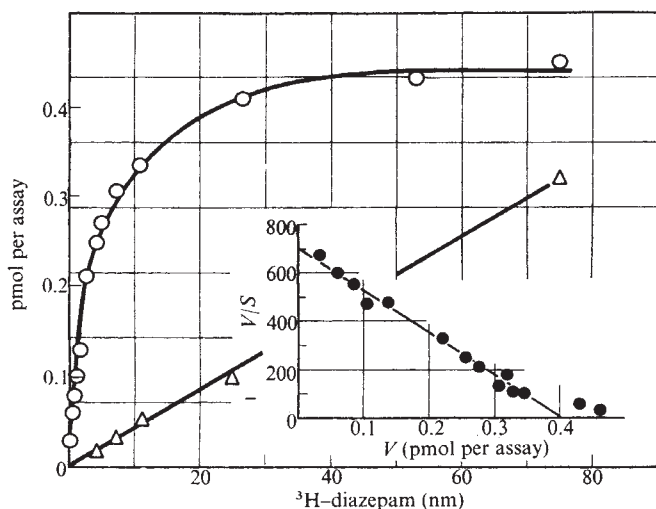


Fig. 1 Binding of ^3H -diazepam to membranes from 25mg rat forebrain. ^3H -diazepam, $0.24\text{--}75\text{ nM}$ was incubated in triplicate with or without excess cold diazepam. Specific binding ($\circ$) is the total binding minus the binding which is not displaced by excess ($3\text{ }\mu\text{M}$) diazepam ($\bullet$). Insert shows the same data transformed to Scatchard plots (V , specific binding in pmol per 25 mg tissue; S , ^3H -diazepam concentration in pM). The Scatchard plot indicates one binding site with affinity constant, $K_D = 2.6\text{ nM}$ (reciprocal of the slope value) and maximal binding of 18 pmol per g original tissue (intercept on abscissae). The experiment was repeated, giving closely similar results. Counting efficiency was 44%.

Measurement of specific ^3H -diazepam binding (at 1.6 nM) in 10 rat brain regions showed an uneven regional distribution. The greatest binding was found in the frontal and occipital cortex where the binding was three to fourfold higher than the lowest binding in the pons-medulla. The hippocampus, which may be an important site of action for benzodiazepines in the limbic system⁴, had intermediate binding levels.

The ^3H -diazepam binding site was highly selective for benzodiazepines. Twenty one benzodiazepines (Table 1) displaced ^3H -diazepam with IC_{50} values in the range of 3×10^{-9} to 10^{-4} M while some other 'minor tranquilisers', such as meprobamate, barbiturates and ethanol, were inactive at 0.1 mM . Several presumed neurotransmitters were tested as ^3H -diazepam displacers. None of these (acetylcholine, noradrenaline, dopamine, serotonin, GABA, L-glutamate or glycine, all at 0.1 mM) or their antagonists (phenoxybenzamine, propranolol, pimozone, clozapine, methysergide, bicuculline, picrotoxin or strychnine, all at $3 \times 10^{-6}\text{ M}$) exhibited any displacement activity. Various other compounds, including etorphine, nalorphine and muscimol (all at $3 \times 10^{-6}\text{ M}$) were also inactive.

Even though the binding of a compound may be saturable and show remarkable selective displacement properties it may not

Table 1 Inhibition of specific ^3H -diazepam binding (1.6 nM) to rat brain membranes by benzodiazepines

Compound*	$\text{IC}_{50}(\text{nM})^\dagger$
RO 5-4023 (clonazepam)	5
RO 5-4200 (flunitrazepam)	5
Lorazepam	7
RO 5-3027	9.2
RO 5-3590	13.1
RO 5-6901 (flurazepam)	28
RO 5-2807 (diazepam)	34
RO 5-3059 (nitrazepam)	34
RO 5-3350 (bromazepam)	48
RO 6-6616 (chlorazepate)	62
RO 5-2904	76
Oxazepam	80
RO 5-2181	135
RO 5-4528	389
Chlordiazepoxide	1,072
RO 5-5807	4,487
RO 5-3785	5,686
RO 5-4556 (medazepam)	6,217
RO 5-3636	8,270
RO 5-4933	<30,000
RO 5-4864	163,522

Serial dilutions of benzodiazepines (in duplicate experiments) were added to the high affinity binding assay (see text).

*Chemical structures given in ref. 6.

$^\dagger\text{IC}_{50}$, concentration causing 50% inhibition of specific ^3H -diazepam binding.

occur at meaningful recognition sites⁵. The diazepam receptor which we describe here, however, seems to be physiologically significant since it can be correlated to pharmacological activities. Efficacies in several pharmacological tests are available for most of the benzodiazepines used in the present study⁶. Excellent correlations ($P > 0.001$) were observed between ^3H -diazepam displacement potency on the one hand and cat muscle relaxant effect, impairment of mouse rotarod performance, inhibition of electric shock induced fighting in mice and antagonism of pentazol induced convulsions in mice, on the other. Weak correlation was found to taming of cynomolgus monkeys ($P = 0.01$, $r = 0.655$). Displacement of ^3H -diazepam binding correlates best with the cat muscle relaxant effect (Fig. 2). While the pharmacological tests listed above are predictive of anxiolytic and anticonvulsant activity we found no correlation with the non-predictive conditioned avoidance tests (either shock increase or escape failures) in the rat.

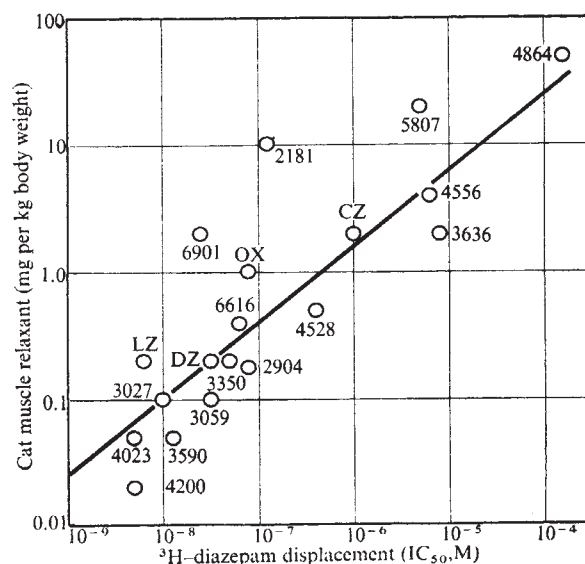


Fig. 2 Correlation between IC_{50} values for ^3H -diazepam displacement by 19 benzodiazepines (from Table 1) and cat muscle relaxant (oral dosage) effect. The best curve fit was assessed by linear regression analysis ($r = 0.891$; $P < 0.001$). Numbers on graph indicate RO code number, OX, oxazepam; DZ, diazepam; LZ, lorazepam; CZ, chlordiazepoxide.

In a comprehensive review, Randall *et al.*⁶ concluded that the 'actions of benzodiazepines cannot be related in a direct manner to the action of neurotransmitters in the brain'. The proposal⁷ that benzodiazepines act on glycine receptors seems now unlikely in view of electrophysiological data^{8,9} and our finding that neither glycine nor its antagonist strychnine displace ³H-diazepam binding. Further, the benzodiazepines were about 10,000 times more potent as displacers of ³H-diazepam binding than ³H-strychnine binding. And ³H-diazepam does not apparently bind to GABA-receptors, since GABA itself, its potent agonist muscimol and its antagonists picrotoxin and bicuculline were completely inactive as ³H-diazepam displacers. The failure of benzodiazepines to block ³H-GABA binding to brain membranes¹⁰ further indicates the lack of direct benzodiazepine interactions with GABA receptors. These results, however, are not inconsistent with the proposal that benzodiazepines exert their physiological effects through GABA¹¹, since such effects may be indirect (for example, benzodiazepines might facilitate GABA release).

Our findings strongly suggest that the brain possesses specific receptors for benzodiazepines which may mediate their pharmacological actions. The exact mechanisms by which benzodiazepines exert their characteristic pharmacological and clinical effects remain unknown. A search for a hitherto undiscovered endogenous transmitter substance, acting on the benzodiazepine receptor therefore seems worthwhile.

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Axotomy causes loss of muscarinic receptors and loss of synaptic contacts in the hypoglossal nucleus

MUSCARINIC receptors in the brain and ileum can be studied by means of the binding of radiolabelled cholinergic antagonists^{1,2}. The basic criteria for receptor-specific labelling are that there should be a saturable component of binding and that the binding of the radiolabelled ligand should be inhibited by pharmacologically effective concentrations of drugs which are known to act at muscarinic receptors and not by drugs that act at different receptors. In addition, the saturable binding component should be restricted to tissues known from pharmacological experiments to contain muscarinic receptors. These criteria are satisfied by tritiated propylbenzilylcholine mustard (³H-PrBCM)³, a potent irreversible muscarinic antagonist the binding of which to rat brain sections can be demonstrated autoradiographically. The evidence which suggests that the bulk of tissue radioactivity is associated with muscarinic receptors is that in

autoradiographs the regional variation of autoradiographic grain density parallels the intensity of specific ³H-PrBCM binding observed by *in vitro* assay on brain homogenates from selected regions, and that in the homogenates 65-85% of the bound radioactivity is blocked by pretreatment with the classical muscarinic antagonist, atropine (10⁻⁶ M). In the forebrain the general features of the distribution of ³H-PrBCM binding to thin sections correspond closely with the findings of Kuhar and Yamamura^{4,5} who used the non-covalently bound antagonist ³H-3-quinuclidinylbenzilate. We report here, however, that in the brain stem the hypoglossal nuclei are heavily labelled with ³H-PrBCM. In light microscopic autoradiographs (Fig. 1a, left side) the grains are distributed throughout the neuropil of the hypoglossal nucleus. The cytoplasm and nuclei of the large hypoglossal neuronal somata (Fig. 1b) are unlabelled. The density of the silver grains falls abruptly at the borders of the hypoglossal neuropil. This clear demarcation of the labelled hypoglossal neuropil is abolished by atropine pretreatment (Fig. 1c).

The present results are based on a total of 48 adult female Wistar rats in which the hypoglossal nerve was cut on one side in the neck. In 30 animals the brains were prepared for light microscopic autoradiographic study of receptor binding, and in a further 18 animals the brains were prepared for an electron microscopic study of synapse numbers.

Several studies⁶⁻⁹ of the effects of axotomy on the hypoglossal nucleus have shown that by 1 week after operation there is a loss of about 50% of the synapses on the hypoglossal motoneurons. If the hypoglossal axons are able to regenerate and re-establish neuromuscular contacts, synapses reappear in the hypoglossal nucleus, indicating that the synaptic 'disjunction' is reversible. We have examined the hypoglossal nucleus at various times after section of the hypoglossal nerve on one side, and the preliminary series of experiments indicated that two changes are detectable within 2 d after axotomy, and seem to have reached completion by 7-10 d after operation.

There was a marked decrease in the intensity of binding of ³H-PrBCM. Since the nerve arises almost exclusively from the hypoglossal nucleus of the same side, and the two nuclei lie immediately adjacent to each other on either side of the midline, the opposite nucleus can be used as a control in the same coronal section. A representative indication of the magnitude of the changes may be seen from the grain counts taken from the sections shown in Fig. 1a and c. The numbers of silver grains per 10⁴ μm² of section were 305±5 over the unoperated hypoglossal nucleus, 209±4 over the hypoglossal nucleus of the operated side (6 d after axotomy), and 123±3 over the hypoglossal nucleus of the unoperated side in the adjacent section (Fig. 1c) pretreated with atropine. Subtracting the atropine counts, this indicates that section of the hypoglossal nerve had caused a fall in the intensity of labelling of the hypoglossal nucleus of the operated side to 47% of its intensity on the unoperated side.

At the electron microscopic level, we counted the total numbers of synapses per unit area of section. As in the studies of Sumner⁷ we found that there was an almost 50% reduction in the total numbers of synapses by 1 week after operation.

If the hypoglossal nerve is able to regenerate and re-establish contact with an appropriate peripheral target tissue, these changes are reversed. The hypoglossal motoneurons re-acquire a normal complement of afferent synapses⁸⁻⁹ and our observations on the rats with the longer survival times showed that in those cases where the hypoglossal nerve had grown back, binding of ³H-PrBCM in the hypoglossal neuropil had also recovered to normal levels. In some animals, the regenerating

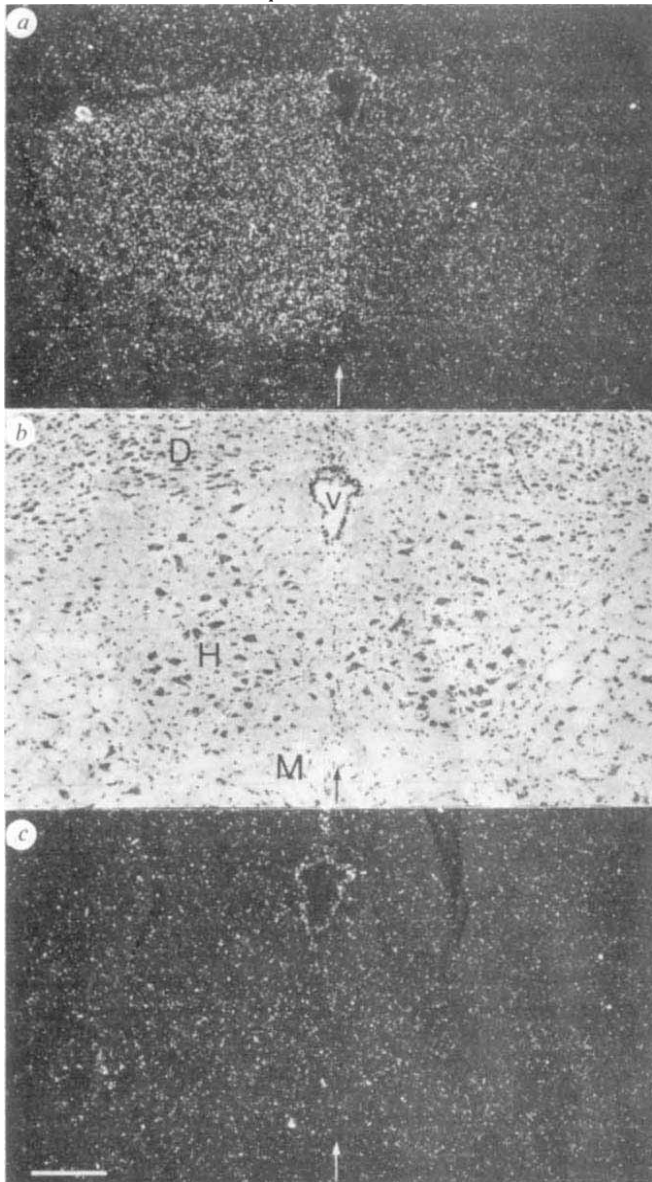


Fig. 1 Coronal sections through the rat brain stem at the level of the caudal medulla, where the hypoglossal nucleus has its major cross sectional area. The arrows show the midline. *a*, Dark field photomicrograph showing the intense deposition of autoradiographic silver grains over the hypoglossal nucleus on the left side of the picture (side of the intact hypoglossal nerve). Labelling falls abruptly at all the boundaries of the hypoglossal neuropil. On the opposite side, where the hypoglossal nerve had been sectioned 6 d previously (right side of the picture), the labelling is 47% of its intensity on the unoperated side. *b*, Bright field photomicrograph of the same section to show the cytoarchitectonic areas. H, hypoglossal nucleus, D, dorsal vagal nucleus, M, medial lemniscus, v, caudal ('closed') part of the fourth ventricle. *c*, Dark field photomicrograph of the adjacent section, which had been pretreated with 10^{-6} M atropine to abolish specific muscarinic antagonist binding. The hypoglossal nucleus shows no labelling above the level of the surrounding areas. Scale bar, 200 μ m. For autoradiographic study of muscarinic receptor binding, the animals were anaesthetised with ether and perfused briefly with ice-cold Krebs–Henseleit medium. The brains were dissected out, frozen in solid carbon dioxide, and mounted on cryostat chucks. Coronal sections (12 μ m thick) were cut at -15°C , thaw-mounted on to gelatinised slides and pre-fixed in 0.1% glutaraldehyde in Krebs–Henseleit medium at 5°C for 15 min. Pre-incubation was carried out for 15 min at 30°C in Krebs–Henseleit medium with or without 10^{-6} M atropine, followed by addition of cyclised ^3H -PrBCM (40 Ci mmol $^{-1}$) to a final concentration of 2.4 nM for a further 15 min; these conditions lead to a more than 98% saturation of the receptors. The incubation was terminated by a quick wash in distilled water and post-fixation in Carnoy's fluid followed by several extensive washes in absolute alcohol. Slides were dipped in a 1:1 dilution of Ilford G5 nuclear emulsion, exposed at 6°C for 14 d, developed in Ilford Phen-X, and counter-stained with cresyl fast violet.

proximal nerve stump had reconnected only incompletely, or not at all to the distal trunk. In these cases, the binding of ^3H -PrBCM had returned only in patches. Sumner¹⁰ has shown that if the cut hypoglossal nerve is not allowed to re-establish peripheral contacts, there is no recovery of synapse numbers. Taken together, these observations indicate that in the case of the hypoglossal motoneurones axotomy causes both loss of synaptic contacts and loss of binding of ^3H -PrBCM, and both these changes are reversed if the axons regenerate appropriate terminal contacts, but not if they fail to do so.

In several sites in muscle^{11,12} and nerve¹³, experimental destruction of the presynaptic element causes postsynaptic cholinergic (nicotinic) receptors to increase in number, and a new population of receptors to appear outside their normally restricted subsynaptic location, indicating that the maintenance of normal receptor number and distribution depends on the presence of the presynaptic element. Although we know of no direct electrophysiological evidence for the occurrence of cholinergic transmission using postsynaptic muscarinic receptors in the hypoglossal nucleus, the occurrence of specific muscarinic antagonist binding strongly suggests the presence of such a mechanism. In the present experiments, damage to the postsynaptic neurone caused a decrease in the amount of binding of muscarinic antagonist, and a loss of synaptic contacts, and our preliminary results from a closely timed series of experiments suggest that the binding loss may precede the loss of synapses. Our method of applying the PrBCM directly to the cut sections makes it likely that the decreased binding is due to a loss of receptors, and not to changes in the accessibility of the receptor (for example by the interposition of a glial barrier).

Taken together with the observation that axotomy causes a decrease in sensitivity to transmitter in several types of neurones (for example see refs 14 and 15), the findings in the hypoglossal nucleus suggest that there could be a converse regulatory relationship—namely that the presence of receptors may be necessary for the maintenance of the physical contact between the pre- and the postsynaptic elements.

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Specific long-lasting potentiation of synaptic transmission in hippocampal slices

SHORT bursts of tetanic stimulation (10–50 Hz for 10–15 s) give rise to long-lasting potentiation (LLP) of synaptic transmission in the intact hippocampal formation¹ and in hippocampal slices². The potentiation may last several hours. Because of the time course and the small number of conditioning impulses required, the process may have general interest as a model for long-term plasticity in the nervous system. Studies of the mechanisms underlying LLP have been hampered, however, by lack of control with the size of the input volley and of data on membrane potential changes of the participating cells. Further, it is not known whether the potentiation is specific for the tetanised input. Schwartzkroin and Wester³ found an unchanged antidromic field potential, and concluded that there were no general postsynaptic changes. Lynch *et al.*³, however, found a reduction in glutamate sensitivity during the potentiated stage, and suggested that a reduction in excitability had taken place. We report here experiments on transverse hippocampal slices⁴ of guinea pigs in which we have monitored the size of two independent afferent inputs, one of which is tetanised to produce LLP, leaving the other as a control line to check for non-specific changes in excitability. Furthermore, intracellular recordings support our suggestion that LLP is caused by a specific augmentation of transmitter release.

Figure 1 shows the location of a typical CA1 neurone with reference to the layers of the hippocampal slice, and the arrangement of the stimulating and recording electrodes used to study two independent pathways, one in the layer of basal dendrites

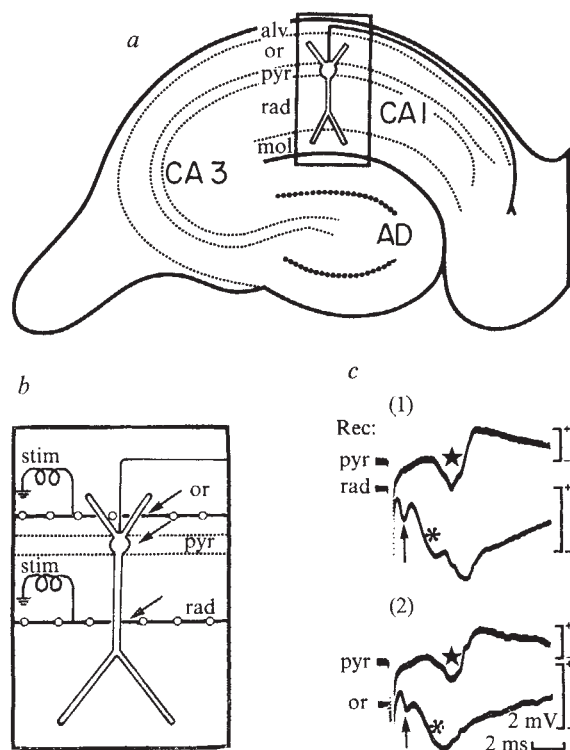


Fig. 1 *a*, Schematic drawing of the hippocampal slice. alv., alveus; or., str. oriens; pyr., str. pyramidale; rad., str. radiatum; mol., str. moleculare. *b*, Enlargement of box in *a* to show the arrangement of stimulating cathodes (stim) and recording electrodes (→) along two independent pathways, one in str. oriens and one in str. radiatum. *c*, Example of recorded potentials showing presynaptic volley (↑), extracellular EPSP (*), and population spike (★) in response to stimulation of a radiatum pathway (1) and an oriens pathway (2). Left-hand labels indicate recording sites.

(str. oriens) and the other in the layer of apical dendrites (str. radiatum). Both excite the CA1 pyramidal cells through fibres running parallel to the pyramidal layer. The fibres have *en passage* boutons which synaptically excite dendrites at the same level as the corresponding stimulating cathode (Fig. 1*b*). Field potentials were recorded with three electrodes, two placed at the same level as the two stimulating cathodes, and the third in the pyramidal layer, all three being placed on a line normal to the pyramidal layer, and recording from the same population of pyramidal neurones. In some experiments, the pyramidal electrode was used for intracellular recording.

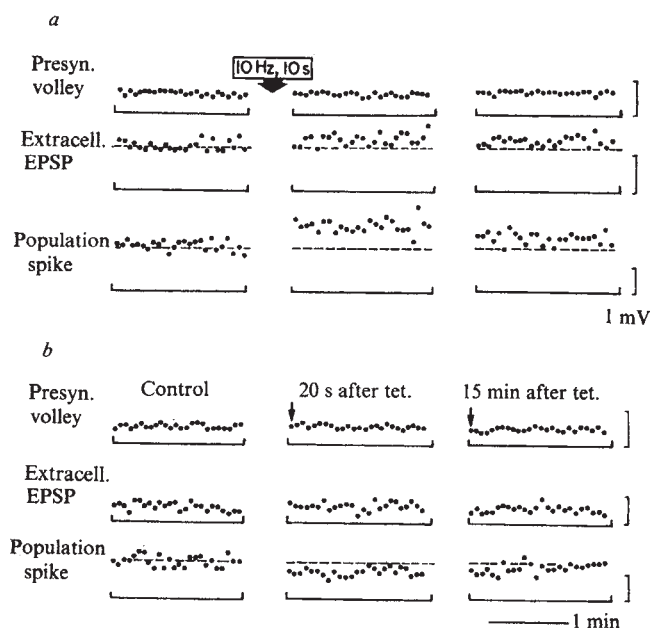


Fig. 2 Left-hand columns in *a* and *b* give control responses before a tetanus of 10 Hz for 10 s was delivered to the radiatum pathway. The middle column shows the responses obtained between 20 and 120 s and the right-hand column shows responses recorded between 15 and 16.7 min after the cessation of the tetanus. *a*, Increased amplitude of the extracellular EPSP in str. radiatum and of the population spike in the pyramidal layer in response to a constant radiatum fibre volley (0.25 Hz, 29 μ A). A small increase of the presynaptic volley is seen in the right-hand plot. *b*, Lack of consistent changes of the amplitude of the presynaptic volley, extracellular EPSP recorded from str. oriens and of the population spike recorded from the pyramidal layer in response to stimulation of oriens fibres (0.25 Hz, 15 μ A).

When a group of fibres was stimulated, the dendritic electrode at the same level recorded an initial diphasic deflection followed by a negative wave with an irregularly shaped peak (Fig. 1*c*). The initial diphasic deflection (↑) is taken as the sign of the presynaptic fibre volley for the following reasons: it was located strictly to the activated level, was linearly related to the EPSP amplitude, showed a conduction velocity of about 0.3 ms⁻¹, followed high-frequency stimulation, and was not changed by removal of Ca²⁺ from the bathing fluid (Andersen, Silfvenius, Sundberg and Wigström, unpublished observations). The following negative extracellular field potential (*) was directly correlated to intracellularly recorded EPSPs and is taken as the extracellular sign of EPSPs from a group of neighbouring cells. Finally, a population spike (★), which represents an envelope of unit discharges⁵, was recorded from the pyramidal layer. The two pathways were stimulated alternately so that each line was tested every fourth second. We measured continuously the size of the presynaptic volley and the corresponding extracellular EPSP. Both may serve a measure of the input strength⁶. Further, we measured the size and peak latency of the population spike. After a control period of 15–30 min, a brief tetanisation was given to one of the pathways (10 Hz for 10 s or 50 Hz for 5 s).

Figure 2 shows synaptic transmission in the radiatum pathway to be greatly facilitated after tetanic stimulation of the same pathway, as indicated by an increased extracellular EPSP and a greatly enhanced population spike with reduced latency. Further, the probability of single unit discharges increased during the period of the enhanced extracellular EPSP. These effects subsided only gradually and could last > 1 h. It proved necessary to monitor the size of the presynaptic volley. In eight of 16 trials a transient increase of this deflection (< 10 min) occurred post-tetanicly. Further, in some experiments, distinct and seemingly spontaneous changes of the presynaptic volley developed. Therefore, to assess the potentiation effects, input-output graphs were produced before and at various times after the tetanisation. Comparing the input-output curves taken before and after the tetanisation, a given afferent volley along the tetanised line gave rise to a larger extracellular EPSP (13 of 16 trials) and a larger (13/13) and shorter latency (12/13) population spike (Fig. 3). In none of the seven trials in which control line responses were measured, were there any observable changes in the latter, except a transitory and small change of the population spike, usually lasting < 3 min. The LLP, therefore, seems to be an input-specific effect.

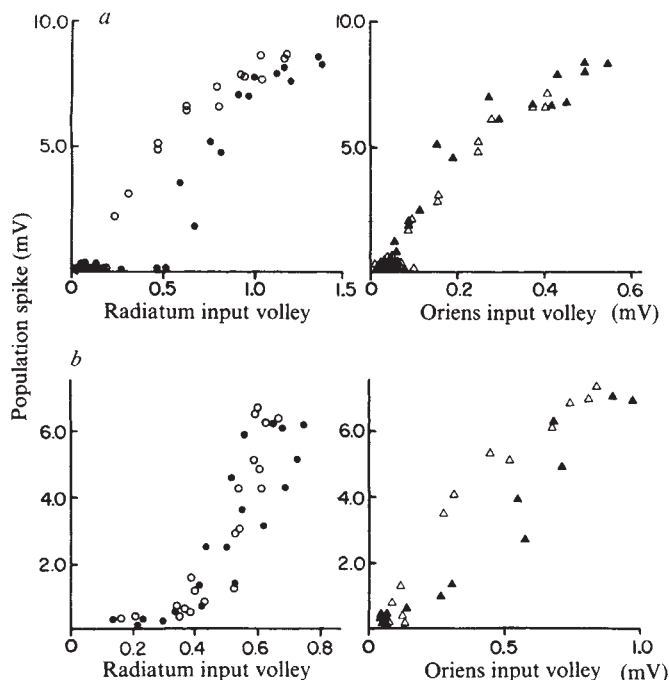


Fig. 3 Input-output graphs for radiatum line (left) and oriens line (right) in two slices. *a*, Slice in which tetanisation (50 Hz, 5 s) was given to str. radiatum. Responses to radiatum stimulation before (●) and after (○) tetanisation and to oriens stimulation before (▲) and after (△) tetanisation. *b*, Symbols as in (*a*) but a different slice and tetanisation (50 Hz, 5 s) now delivered to str. oriens.

We also compared the size of the presynaptic volley and the probability of discharge of single CA1 neurones. The input-output graphs changed after the tetanus in the same way as for the population spike. With intracellular recording the membrane potential, the size of the EPSP and the firing threshold of the spike were compared pre- and post-tetanicly. In Fig. 4, three afferent volley sizes produce a larger EPSP after the tetanisation than before. The increased EPSP caused the spike to occur in response to a smaller input volley and with a shorter latency compared to the pre-tetanic values. The fact that the membrane potential did not change suggests that the increased EPSP is due to an augmented transmitter release. In these experiments we did not systematically test the spike threshold by injecting depolarising current pulses in the soma because this threshold was found to be the same as the threshold for synaptically activated spikes.

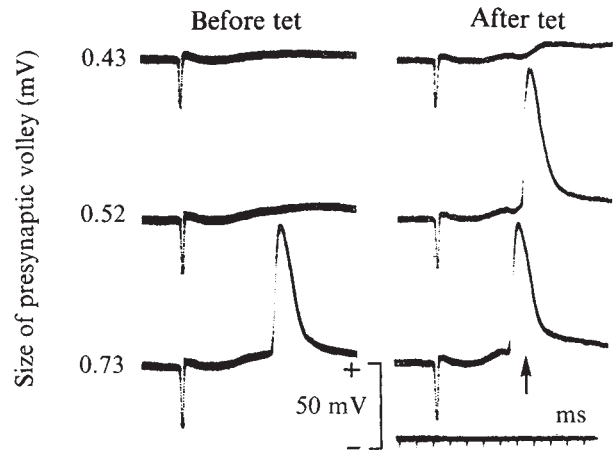


Fig. 4 Intracellular recording of responses to three differently sized radiatum fibre volleys. The peak-to-peak size of the volleys are given in mV on the left. Left-hand column were taken before, right-hand column 15 min after a 50 Hz, 5 s tetanus was delivered to the same radiatum fibres. After the tetanus a given input volley gives a larger and faster rising EPSP and increased probability of firing and a reduced latency. No significant change in the membrane potential occurred except during and shortly after the tetanus. Neither was there any change in the firing level of the action potential. The arrow indicates the latency of the control spike.

The claim for an input-specific process underlying the LLP rests on our observation of unchanged control line responses. Admittedly, small changes of these were seen, but an increase in excitability were as likely as a decrease, and both were unrelated to the tetanisation. Our failure to observe systematic changes in the control line responses makes it difficult to ascribe the reduced glutamate sensitivity seen during LLP to a general depression of post-synaptic excitability as done by Lynch *et al.*³.

In conclusion, we believe the presented evidence suggests that short tetani of fibres having dendritic synapses on CA1 hippocampal pyramids lead to an input-specific and long-lasting potentiation (LLP) of synaptic transmission. The effect is hardly due to changes in the afferent volley since our method allows control of the latter. Because unwanted changes in the input volley can occur, we feel that experiments on LLP require adequate input control.

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Heterosynaptic depression: a postsynaptic correlate of long-term potentiation

BRIEF trains of electrical stimulation delivered to any one of several hippocampal pathways often result in immediate and long-lasting enhancement of subsequent postsynaptic

responses elicited by that pathway¹⁻⁵. The unusual characteristics of these effects suggest that theories of long-term potentiation (specifically changes in transmitter release by the presynaptic terminal) which have evolved from work on invertebrate and neuromuscular preparations may not be appropriate to explain synaptic plasticity in hippocampus. We report here the results of experiments intended to examine the postsynaptic consequences of repetitive stimulation. We found that potentiation of one afferent tended to depress the target cell's responses to a second test input.

We used the *in vitro* hippocampal slice technique, details of which have been published^{6,7}. Briefly, rats were stunned, the hippocampus rapidly dissected free, and then sliced at right angles to its longitudinal axis on a Sorvall tissue chopper. The slices (500 μ m thick) were then transferred to a small recording chamber of our design⁷ and immersed in a slightly modified glucose-Ringer solution. All experiments were run at 33 °C.

Figure 1 shows the experimental design. The CA1 field was chosen for the analysis because it receives two different inputs to completely different dendritic subfields—namely, the apical and basal dendritic fields. Because of this anatomical arrangement, it is relatively easy to study the interaction of two spatially separate afferents on the same postsynaptic neurones. One bipolar stimulating electrode (twisted 62- μ m wire) was placed in the trajectory of the Schaffer collateral-'apical' commissural projections to the stratum radiatum of the CA1 pyramidal cells. A second bipolar electrode was localised in the stratum oriens of the CA1, a zone which contains a massive commissural projection to the basal dendrites of the CA1 cells^{8,9}. A recording micropipette was then guided by visual landmarks and physiological responses (cell spikes) into the pyramidal cell body layer (stratum pyramidale). The distances between stimulating and recording electrodes were typically 1–3.0 mm. A total of 28 slices was tested.

Low voltage stimulation to these pathways produced the responses characteristic of the laminated hippocampal projections—a monophasic negative-going potential in the dendritic zone innervated by the stimulated afferent and a monophasic positive potential in the stratum pyramidale. The response was similarly positive but considerably attenuated in the dendritic zone across the cell body layer from the stimulated afferent. As voltage was increased the 'dendritic' negative potential grew larger and a prominent

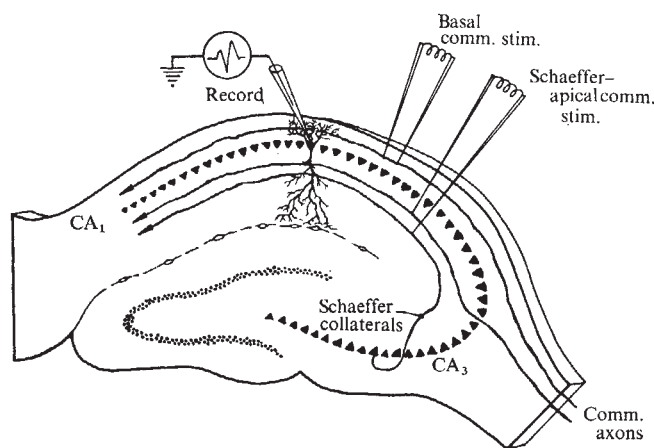


Fig. 1 A schematic diagram of the transverse hippocampal slice illustrating the experimental arrangement. Stimulating electrodes have been placed in two pathways as they enter the CA1 subfield. These are the commissural fibres occupying the basal dendritic area and the mixed input of Schaffer collateral-commissural fibres occupying the apical dendrites of these neurones. Sites of stimulation were chosen to ensure that the commissural fibres stimulated by each of the electrodes would be unique to that zone.

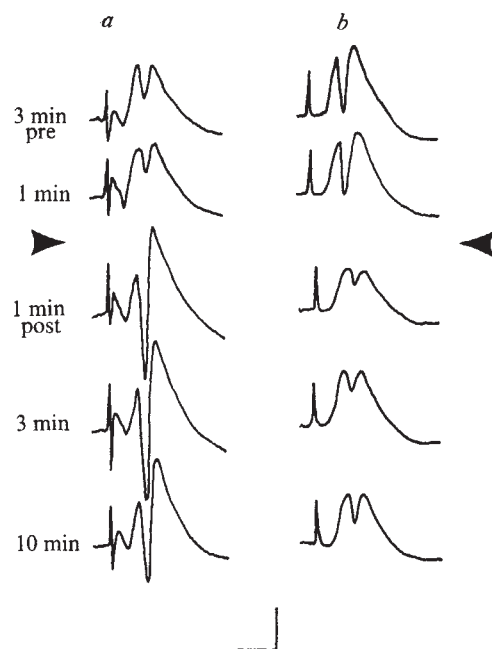


Fig. 2 An example of the depression seen in the commissural response (*b*) concomitant with post-tetanic potentiation of the Schaffer response (*a*). Note that all aspects of the commissural evoked response exhibit depression. The component most drastically reduced is the negative population spike, while the Schaffer population spike shows the greatest degree of potentiation following tetany. The potentiation stimulus consisted of a 15-Hz, 15-s train delivered (at test voltage) through the Schaffer electrode at the arrows. All records are an average of four responses; the test frequency was 0.2 Hz, pulse duration was 0.1 ms. Vertical scale, 1 mV; horizontal scale, 5 ms.

sharp negative deflection appeared in the positive response recorded from the cell bodies. This negative potential is likely to be generated by the synchronous spike discharge of several pyramidal cells, as shown by Anderson *et al.*¹⁰, and, following their terminology, we refer to it as a 'population spike'.

Following the placement of the three electrodes, the size of the responses evoked by the two electrodes was made approximately equal by adjustments of the stimulating voltages (usually 5–10 V). The voltages selected were adequate to generate a small (1 mV) population spike. The responses in both pathways were periodically tested with trains of four pulses presented at 0.2 Hz during a 5–10-min pretest. If these remained stable, a brief train (2–15 s) of 15-Hz stimulation was delivered to one of the two electrodes, then the frequency was returned to 0.2 Hz. In most experiments, the magnitude of the conditioning and test responses was sampled at 1-min intervals post-potentiation by averaging trains of four pulses given at 0.2 Hz. The potentiation train was delivered to the 'Schaffer' electrode in 13 slices and to the 'commissural' electrode in 15 cases.

During the stimulation train both the conditioning and test responses (that is, the responses to the electrodes which received the 15-Hz train and to the one which did not, respectively) were greatly augmented. After the termination of the train the two responses behaved quite differently. In 26 of 28 of the slices, the response elicited by the electrode which had delivered the high-frequency train was potentiated, particularly with regard to the population spike. This facilitation usually was evident within one or two pulses after the train and persisted for at least 15 min. Responses to stimulation in the non-potentiated pathway declined rapidly (over 15 s) towards baseline following repetitive stimulation of the other electrode, and in 22 of the cases entered a period of persistent depression (mean size of the population spikes tested at 2 min post-conditioning train was 68% of the control value ($P < 0.001$) (Fig. 2 and see

Fig. 3). As was the case for potentiation, the depression was more evident in the population spike than in the slower field potentials.

Thirteen of the slices were tested for longer post-tetani periods and both potentiation and depression lasted for at least 15 min (Table 1). To test for effects longer than this it would be necessary to establish control procedures to insure that the status of the preparation remained stable for longer periods.

In these 13 slices we also delivered a tetanic train of stimulation to the depressed pathway, usually at 16 min after the first potentiation train. In all but one of these cases the depressed response showed marked potentiation, whereas in every case the previously potentiated responses were depressed (averages were 327% and 76% of the immediate pre-tetanus response 2 min following the reversal train).

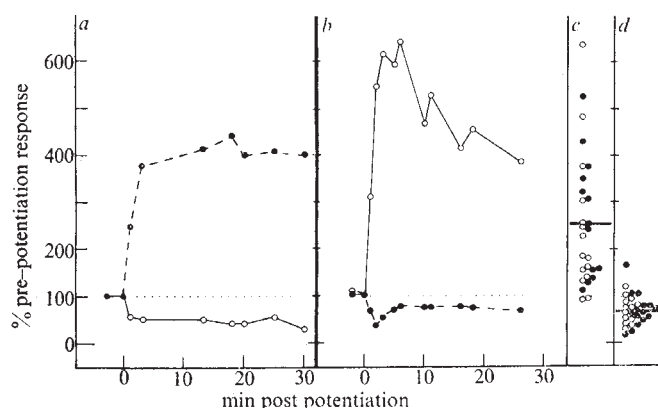


Fig. 3 Amplitude plot of the population spike evoked by both stimulating electrodes during 0.2-Hz 'test' stimulation. The figure shows the size of the population spikes both before and after a 15-Hz, 15-s train was delivered to either the Schaffer (a) or commissural (b) afferents at time 0 (different slices). c and d show potentiation and depression, respectively, of a group of slices whose responses were tested at 2 min after the potentiating train. Amplitudes are plotted as the percentage of the last non-potentiated response. Schaffer responses indicated by solid circles and commissural responses by open circles. Bars indicate means.

It seemed that, for most slices, long-term potentiation of one input to the pyramidal cells was accompanied by an unusually persistent depression of the response to remaining inputs. As the anatomical arrangements of the slice and the afferents used in this experiment are such as to make any axo-axonic interactions highly unlikely, our results suggest that brief trains of 10–15 Hz stimulation lead to two effects: (1) a local enhancement or potentiation of the driven afferent and (2) a generalised depression of the postsynaptic neurones.

Other lines of evidence also suggest that repetitive stimulation leads to some type of persistent and generalised depression of the postsynaptic cells. We have reported elsewhere¹¹ that long-term potentiation is accompanied by a persistent decrease in cell firing in response to glutamic acid applied by iontophoresis to the dendrites of the CA1 pyramidal cell.

Table 1 Comparison of population spike amplitude before and after tetanic stimulation

	Pre	Minutes post tetanus		
		5	10	15
Tetanis pathway	100%	390%	380%	332%
Control pathway	100%	74%	67%	73%
	N = 17	N = 17	N = 17	N = 13

All post-tetanic values were significantly different ($P < 0.05$) from immediate pre-tetanus values, as determined by a matched-pairs signed-ranks test.

In the absence of intracellular recordings we cannot dismiss the possibility that two intermingled sets of neurones are involved in the two effects, that the potentiation is localised to one set of cells and the depression to another. This seems unlikely, as it is quite evident from extracellular recordings that the same cells are driven by the two afferents used in our experiments. But whether we are considering opposing effects on a single neurone or in a small population of cells the present findings suggest that a kind of physiological modelling may go on in the hippocampus in which one afferent through repetitive firing gains at least a temporary priority at the expense of its neighbours. Finally, our results indicate that potentiation or depression of a pathway does not diminish the capacity of that system to undergo further plastic changes in response to subsequent episodes of repetitive stimulation.

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Ethanol reduces excitatory postsynaptic current duration at a crustacean neuromuscular junction

ETHANOL potentiates the postsynaptic voltage response to acetylcholine at mammalian and amphibian neuromuscular junctions^{1–4}, by prolonging the duration of the postsynaptic conductance change^{5–7}. At these synapses, hyperpolarisation also increases the time constant of decay (τ) of end-plate currents^{8–14}. Because of this voltage sensitivity, it was proposed¹⁵ that the rate-limiting reaction in the decay of end-plate currents involves the relaxation of membrane proteins, which undergo a change in dipole moment normal to the field direction as they change conformation. The magnitude and direction of the change in dipole moment then determines the effect of electric field on α , the reaction rate. α ($=\tau^{-1}$) would be proportional to $\exp(V\mu)$ (ref. 15) where V is membrane potential and μ the dipole moment change normal to the field direction. It has been suggested that the prolonged decay of end-plate currents produced by ethanol is due to increase by ethanol of the dielectric constant of the environment of receptors⁶, which lowers the rate of reactions involving a decrease in dipole moment¹⁶ and hence increases τ . In some arthropods, including crayfish, crab and locust, there is evidence that glutamate acts as an excitatory transmitter at neuromuscular junctions^{17,18}. Also, the decay of excitatory postsynaptic currents in crayfish¹⁹ and locusts²⁰ has the opposite voltage sensitivity to that found at amphibian neuromuscular junctions: hyperpolarisation reduces τ , suggesting that the rate-limiting reaction in the decay of conductance at these 'glutamate' synapses could be associated with a change in dipole moment which is opposite to that seen at amphibian neuromuscular junctions. Ethanol could

then have an opposite effect at these two types of synapse, and depress synaptic transmission at glutamate synapses. We report here results of our study of spontaneous miniature excitatory junctional currents (MEJCs) in the crab, which confirm this hypothesis.

We studied the opener muscle (abductor of the dactyl) of the walking legs of the crab (*Scylla serrata*). Dissected muscles were continuously perfused with crab solution containing 466 mM NaCl, 8 mM KCl, 20 mM CaCl_2 , 12 mM MgCl_2 and 10 mM NaHCO_3 , pH 7.45 (ref. 21). Temperature was controlled to within 0.5 °C in the range 10–22 °C. The time course of decay of MEJCs was determined by recording extracellular potentials with low resistance (0.2–1 M Ω) electrodes (filled with 1 M NaCl) which were located focally over junctional regions. In some experiments, intracellular microelectrodes (3 M KCl) were used simultaneously to record membrane potential. MEJCs, which occurred at a low frequency (sometimes $> 1 \text{ min}^{-1}$) were recorded (using a Neurograph-N3 digital transient recorder), displayed on an oscilloscope screen and photographed.

Although the shape and duration of MEJCs varied, two distinct types were recorded. The 'fast' MEJCs examined here had a rapid growth phase (0.2–0.5 ms), then a slower decay lasting 2–5 ms at 20 °C (Fig. 1A). The other, 'slow' MEJCs, not studied here, had a variable, slower growth phase followed by a much slower,

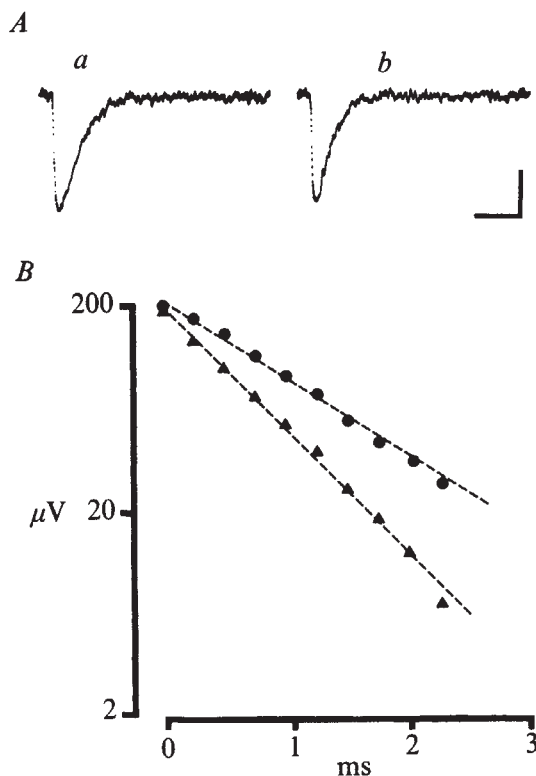


Fig. 1 Ethanol increases the rate of decay of MEJCs. *A*, MEJCs recorded in normal crab solution (*a*) and in the presence of 0.25 M ethanol (*b*). Calibrations: vertical, 100 μV ; horizontal, 2 ms. *B*, semilogarithmic plot of the decay of MEJCs in control solution (●) and in 0.25 M ethanol (▲).

non-exponential decay phase lasting < 50 ms. The decay of most of the fast MEJCs could be described by a single exponential function, as at amphibian neuromuscular junctions (Fig. 1B)^{11,12,22}. Similar MEJCs recorded from crab neuromuscular junctions have been described previously^{23,24}.

Recordings of these MEJCs were obtained in six preparations from cells with resting membrane potentials of -65 to -75 mV. The mean time constant of decay (τ) at 20 °C was 1.2 ± 0.05 ms

(mean $\pm$ s.e.m.). The time constant of decay was temperature-sensitive, having a Q_{10} of approximately 2.0 in the temperature range 12–22 °C. The latter observation suggests that the decay of MEJCs is not rate-limited by diffusional loss of transmitter, a process which would be expected to have a lower Q_{10} . Ethanol (0.25 M) caused an obvious and reversible decrease in τ which is illustrated (trace (*b*) in Fig. 1A. The decay of MEJCs in ethanol remained exponential (Fig. 1B). In 0.25 M ethanol, τ was reduced from 1.2 ± 0.05 to 0.5 ± 0.02 ms, a 58% reduction. Lower concentrations of ethanol produced a smaller reduction in τ . The concentrations tested did not significantly change the membrane potential of the muscle fibres. Concentrations of ethanol, which at amphibian and mammalian neuromuscular junctions cause a significant increase in the duration of postsynaptic currents^{5–7}, produce a significant decrease in the duration of postsynaptic currents at crab neuromuscular junctions.

The results are consistent with the idea that effect of ethanol on the time course of postsynaptic currents is related to the change in dipole moment of the receptor during the reaction. The opposite voltage sensitivity of τ seen at glutamate-sensitive synapses^{19,20} could reflect opposite changes in dipole moment, and this could be the explanation for the opposite effects of ethanol. There is no direct evidence for the same voltage sensitivity at the crab neuromuscular junction, but in preliminary experiments we observed that the rate of decay of MEJCs is slowed when the membrane is depolarised by increasing extracellular potassium concentration. It can be calculated⁶ that an increase in dipole moment of about 40 debye in relaxing receptors would give the voltage sensitivity of τ seen at locust neuromuscular junctions²⁰. This is similar in magnitude but in the opposite direction to the change in dipole moment calculated for amphibian neuromuscular junctions⁶. At toad neuromuscular junctions, 0.1 and 0.25 M ethanol increase τ by factors of 1.4 and 2.1, respectively⁶. It is interesting that at the crab neuromuscular junction we find that these concentrations of ethanol reduce τ by factors of 1.7 and 2.3, respectively. This agreement further supports the idea that ethanol could have a similar action at the two synapses, but that the sign of the change in dipole moment determines whether τ is increased or decreased. This explanation is not unique, and there are other possible ways in which ethanol could influence the rate of decay of synaptic currents differently at the two sites, for instance, by affecting differently the rate of dissociation of acetylcholine and glutamate from receptors if these reactions are rate-limiting.

The observation that ethanol can decrease τ at some synapses is interesting, as varied and selective actions of ethanol have been described previously in vertebrate and invertebrate nervous systems: ethanol potentiates cholinergic transmission at the amphibian and mammalian neuromuscular junction^{1–4}, and, conversely, has been shown to depress excitatory postsynaptic potentials in molluscan neurones^{25,26}. It may be relevant that hyperpolarisation has been reported to increase the rate of decay of excitatory postsynaptic currents at some synapses in molluscan ganglia²⁷. Ethanol also selectively depresses certain excitatory synapses in the central nervous system of goldfish without affecting other inhibitory and excitatory inputs²⁸, and depresses both inhibition and excitation of cat spinal motoneurones²⁹. These depressant effects could arise from an increase in the rate of decay of postsynaptic currents, as seen at the crab neuromuscular junction. The reduction in amplitude of excitatory postsynaptic potentials caused by ethanol in molluscan neurones is associated with a reduction in their time to peak²⁶, probably due to an increase in the rate of decay of the underlying currents³⁰.

It is recognised that ethanol has anaesthetic properties. As many general anaesthetics reduce the time constant of decay of end-plate currents in amphibia and mammals, it has been suggested^{31–33} that they may cause anaesthesia through a similar action in the central nervous system, that is, depression of synaptic transmission caused by a decrease in the duration of synaptic currents. A difficulty with this hypothesis has been that ethanol prolongs postsynaptic currents at the motor end-plate. We have now shown, however, that ethanol can reduce the duration of postsynaptic currents and hence depress transmission at a synapse where the transmitter is other than acetylcholine.

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Asymmetrical currents and sodium currents in Ranvier nodes exposed to DDT

THE non-linear component of the capacity current (asymmetrical 'displacement current') of nerve membranes has been thought^{1–3} to result from the movement of intrinsic membrane charges gating the specific pathways for sodium ions ('Na channels'). This interpretation is partly based on the observation that the voltage-dependent relaxation time constants of the sodium activating mechanism roughly agree with those of the displacement currents. According to this hypothesis, a similar correlation should be demonstrated when the kinetics characteristics of the Na system are modified under controlled experimental conditions. In this respect, the insecticide DDT is a useful tool as it slows down the turning-off of the Na-permeability of the nodal membrane^{4,5} without changing the rate of its turning-on. We have therefore compared the relaxation time constants of both the sodium current activation and the displacement current on DDT-treated Ranvier nodes. The results suggest that the intramembrane charge movement is not the sole transition involved in the gating process of the Na channels.

Experiments were carried out on voltage clamped myelinated fibres of the frog *Rana esculenta*. The delayed K current was abolished by tetraethylammonium (TEA, 10 mM) and by replacing the axoplasmic K content by caesium. The displacement currents (I_d), recorded in the presence of tetrodotoxin (TTX, 10^{-6} M), were obtained by subtracting the linear (leakage and capacity) current components in response to hyperpolarising voltage pulses from the responses to symmetrical depolarisations. Fifteen identical pulses were alternatively applied in both directions (starting from a holding potential of $E = -100$ mV) and the corresponding currents were digitised and averaged. DDT, first dissolved in ethanol, was diluted to 10^{-4} M in Ringer solution. Ethanol was present in the final DDT-test solution at a concentration of 2%, so was added at the

same concentration, to the 'control solution' (Ringer + TEA + ethanol 2%). As a rule, the sodium current (I_{Na}) and the displacement currents (I_d) were first recorded in the reference solutions (control solution without and with TTX respectively). The nodes were then superfused with DDT-test solution for 20 min and the I_{Na} records were taken. Immediately afterwards, the TTX-control solution was re-admitted into the chamber and I_d was recorded. Taking advantage of the irreversibility of the DDT effects⁶, this latter procedure permitted measurement of both I_{Na} and I_d after the same time of exposure to DDT. At the end of the experiment, the ability of the nodes to conduct I_{Na} and the persistence of the DDT effects were verified in the control solution.

In our experimental conditions, the effects of DDT on I_{Na} were in good agreement with those previously reported^{4,5}. For reference, Na current records are presented in Fig. 1 *a* and *b*. They confirm that a long-lasting tail of Na current remains after repolarisation, indicating that in DDT-poisoned nodes a fraction of the Na channels remain activated for a long time. The time course of both the turning-on and the turning-off of the I_{Na} activation were plotted against time, assuming that I_{Na} is proportional to the m^2h product (Hodgkin-Huxley variables). The turning-on of the sodium activation is described by a single exponential function with a time-constant

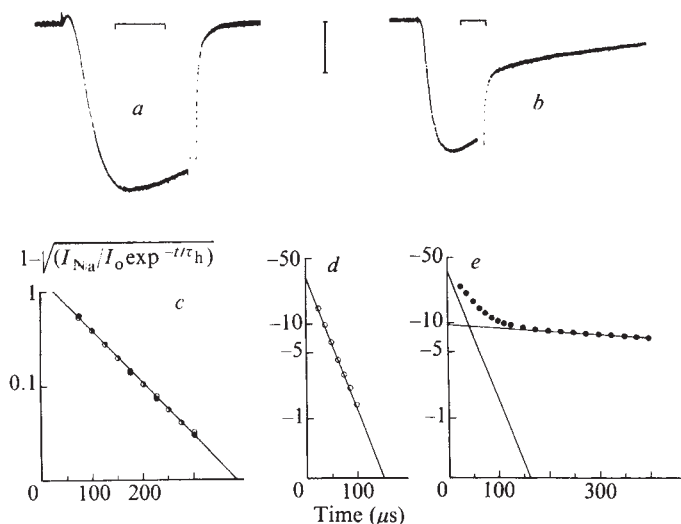


Fig. 1 Sodium current during 100 mV depolarising pulses from a holding potential of -100 mV. *a*, Before DDT and *b*, after exposure to DDT. Capacity and leakage currents were compensated analogically. Vertical and horizontal bars represent 5 nA and 200 μ s respectively. Note the large tail of inward current in (*b*). The difference in the Na-current peak amplitude in (*a*) and (*b*) was not regularly observed. Graphs *c*, *d*, *e* are semilogarithmic plots obtained from the current records (*a*) and (*b*). At the onset of the depolarisation (*c*), before DDT ($\circ$) and after DDT ($\bullet$). At repolarisation to the holding level, before DDT (*d*), after DDT (*e*). The straight lines in (*b*) represent the two exponential components giving the best fit to experimental points. Time constants of the single exponential functions: $\tau_m = 85$ μ s (*c*); $\tau_{Na\text{off}} = 31$ μ s (*d*); $\tau_{Na\text{off},1} = 32$ μ s (fast component in *e*); $\tau_{Na\text{off},2} = 1390$ μ s (slow component in *e*). Temperature 12 $^{\circ}$ C.

$\tau_m = 85$ μ s which is unaffected by DDT (Fig. 1*c*). Under normal conditions (Fig. 1*d*) the turning-off can also be described by a single exponential with another time constant $\tau_{Na\text{off}} = 31$ μ s. When DDT is added to the external medium (Fig. 1*e*), the tail of Na current is fitted by the sum of two exponentials: a fast one ($\tau_{Na\text{off},1} = 32$ μ s) very similar to that of Fig. 1*d*, and a much slower one ($\tau_{Na\text{off},2} = 1390$ μ s). This indicates that a fraction of the channels is unaffected by DDT whereas the rate of turning-off of the other fraction is nearly 45 times slower. From the extrapolated values of I_{Na} to time zero (t_0) in Fig. 1*e*, it may be deduced that, at the end of the

depolarising pulse, 21.4% of the channels were affected in this experiment.

Figures 2a and b represent the displacement currents obtained from the same fibre and at the same membrane potential as in Fig. 1. The analysis of these currents reveals that DDT does not affect the on-response of the displacement current (Fig. 2c) as expected from the results presented in Fig. 1c. However, the time constant $\tau_{d, on} = 113 \mu s$ is 1.3 larger than τ_m . Furthermore, the amount of displaced charges [$Q_{on} = I_{d, to} \tau_{d, on} (1 - e^{-t/\tau_{d, on}})$] is estimated to be 71 fC and is unaffected by DDT. In the absence of this agent (Fig. 2d) the time constant $\tau_{d, off}$ of the displacement current at the repolarisation is 42 μs (that is, 1.3 times larger than

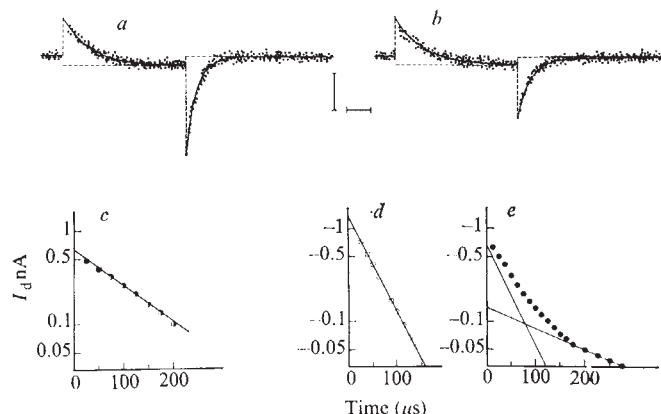


Fig. 2 Averaged displacement currents obtained from the same fibre as in Fig. 1 in response to 100 mV depolarising and hyperpolarising pulses from a holding potential of -100 mV. *a*, Before DDT and *b*, after DDT. Vertical and horizontal calibrations: 0.5 nA and 100 μs . The lines through the points represent the mean values taken as reference for the analysis presented in (*c*), (*d*) and (*e*). The small inward current component during the pulses is probably due to non-linearity of the leakage current between $E = 0$ and $E = -200$ mV or to discrete anodal breakdown during the hyperpolarising pulses; for this reason the zero-current reference for the on-response was taken at the end of the pulses. Graphs *c*, *d* and *e* are semilogarithmic plots of the I_d on (*c*) and off (*d*, *e*) responses, before DDT ($\circ$) and after DDT ($\bullet$). The straight lines in (*e*) represent the two exponential functions: $\tau_{d, on} = 113 \mu s$ (*c*); $\tau_{d, off} = 42 \mu s$ (*d*); $\tau_{d, off, 1} = 42 \mu s$ (fast component in *e*); $\tau_{d, off, 2} = 190 \mu s$ (slow component in *e*). Estimated amount of displaced charges: $Q_{on} = 71$ fC (*c*); $Q_{off} = 55.3$ fC (*d*); $Q_{off, 1} = 28$ fC (fast component in *e*); $Q_{off, 2} = 27.2$ fC (slow component in *e*). Temperature $12^\circ C$.

the corresponding Na_{off}). The amount of transferred charges ($Q_{off} = I_{d, to} \times \tau_{d, off} = 55$ fC) is smaller than that transferred at the onset of the depolarisation. After exposure to DDT (Fig. 2e), two exponential components can be distinguished in the I_d off-response: a fast one ($\tau_{d, off, 1} = 42 \mu s$), similar to that obtained from the control experiment, and a second one, markedly slower, with a time constant $\tau_{d, off, 2} = 190 \mu s$. This second component is supposed to correspond to the fraction of charges affected by DDT. The best fit to the averaged points in the record of Fig. 2b leads to an estimate of the fractions of transferred charges ($Q_{off, 1}$ and $Q_{off, 2}$) of 28 fC (unaffected) and 27 fC (affected by DDT) respectively. The sum of both (55 fC) is identical to the amount of charges displaced at repolarisation under normal conditions.

From a qualitative point of view, the effects of DDT on the displacement currents are those expected from the analysis of the sodium current, in particular when considering that DDT leaves the on-responses unchanged while the off-responses are altered. Thus, our results support the idea that the displacement current reflects the movement of charges involved in the activation process of the Na-conductance. Moreover, it appears that DDT acts only on charges previously displaced by depolarisation and at the time of reversion to their resting state (or position).

The fact that the fraction of charges affected by DDT (50% of the total amount in the experiment reported here) is larger

than the fraction of affected channels (21%) is consistent with the assumption that at least two independent charges are involved in the gating subunit of each channel. If one assumes two particles per channel, only the channels in which both charged particles are affected by DDT will close slowly; those in which only one particle is affected will close at the same rate as intact channels.

A striking result is the observation that DDT increases the relaxation time constant of the I_d off-response by a factor of only 4.5 whereas it enhances that of the Na current by a factor of about 45. This indicates that the channels remain open for an appreciable time after the reversion of the gating charges to their resting configuration. This may be due to a specific effect of DDT. Disagreements between $\tau_{d, off}$ and $\tau_{Na, off}$ have been also observed, however, in squid axons submitted to external solutions made with heavy water⁶. Furthermore, discrepancies between the voltage dependence of the *m*-process and the displacement current have been reported for the squid axon⁶ as well as for the Ranvier node⁷ under normal conditions. There is thus good reason to suppose that DDT exaggerates the relaxation time of a further transition^{6,8}, complementary to the charge displacement and necessary for the closing of the Na channels.

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Effect of transplantation of pancreas on development of hypothalamic obesity

HYPOTHALAMIC obesity is a syndrome of hyperphagia and obesity that follows destruction of the ventromedial region of the hypothalamus. This syndrome is associated with loss of normal nocturnal rise in food intake and with several endocrine changes of which increased concentrations of insulin are the most important. It remains to be settled, however, whether the hyperphagia or hyperinsulinaemia is the primary factor in the development of hypothalamic obesity. The aim of the present experiment was to distinguish between these possibilities by freeing the insulin-secreting islets of Langerhans from neural control. This was done by implanting foetal pancreatic tissue under the kidney capsule of diabetic rats. This experiment prevented the characteristic hyperphagia and obesity seen in the control animals with normally innervated pancreatic tissue. Obesity can be produced by several experimental procedures¹. Among the most widely studied is the one due to damage to the ventromedial region of the hypothalamus^{2,3}. For many years, hypothalamic obesity was ascribed to the destruction of a 'satiety centre' which was thought to coincide anatomically with the ventromedial nucleus of the hypothalamus⁴. Ablation of this 'satiety centre' was believed to remove the inhibitory influences from a primary feeding centre in the lateral hypothalamus and allow excess feeding.

Recent investigations have suggested, however, that this interpretation may be incorrect^{5,6}, and alternative hypotheses have been proposed. One of these suggests that the increase in food intake and obesity are both secondary to the rise in insulin levels which follow ventromedial hypothalamic (VMH) injury. The present studies were designed to critically examine this hypothesis.

An increase in the concentration of serum insulin after a VMH lesion is among the earliest observed changes^{7,8}, and occurs even when the food intake is limited and the increase in body weight is prevented^{9,10}. If the increase in insulin is inhibited by destroying the β cells in the pancreas which produce insulin, the effects of a ventromedial hypothalamic lesion on food intake and body weight are abolished or largely reduced^{11,12}. In addition, it is well known that injections of insulin will increase food intake and body weight¹³. This constellation of findings suggests an important role for insulin, but leaves unsettled the mechanism for its increase. Two possible hypotheses may be advanced. One is humoral, postulating that a 'hypothalamic factor' is released into the circulation and directly stimulates the release of insulin^{14,15}. The other hypothesis proposes a neural mechanism¹⁶. A critical test of these two hypotheses might result from placing hypothalamic lesions in rats whose pancreatic islets were no longer under the neural influences of the pancreatic bed.

Female rats of the highly inbred Lewis strain weighing approximately 200 g were injected with streptozotocin (65 mg kg⁻¹). Four to seven days later, the diabetic rats (overnight fasting blood glucose levels >250 mg dl⁻¹) received transplants of pancreatic tissue from six foetuses which averaged 16–17 d old¹⁷. These transplants were placed beneath the renal capsule and the animals were observed for 4 weeks. The rats with effective transplants showed a gradual decline in serum and urine glucose and the insulin requirement disappeared. After 3 weeks of normal serum glucose, the recovered rats were tested for the function of the transplanted pancreatic tissue by giving them an intraperitoneal challenge with glucose (1 g kg⁻¹). The increase in serum glucose was similar in transplanted and control animals. Bilateral ventromedial hypothalamic lesions or sham-operations were introduced in the transplanted and control animals. Bilateral ventromedial hypothalamic lesions were produced using previously described coordinates¹⁸ (at the Bregma anteriorly; ± 0.7 mm lateral to midsagittal line; and 1.0 mm above the base of the skull). Six of the eight control (non-transplanted) rats and five of the seven rats with pancreatic transplants had adequate hypothalamic lesions as confirmed by histological examination of stained sections of the brain. Data on body weight, the Lee index for body fatness at the final week and food intake measured two weeks after VMH lesions were compared using an analysis of variance with multiple range comparisons.

Body weight rose an average of 120 g in the lesioned rats with normal pancreatic tissue (Fig. 1) and reached an

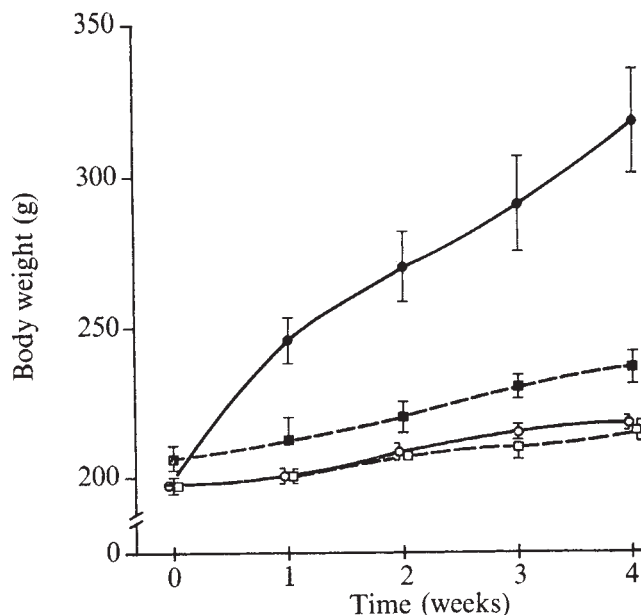


Fig. 1 Body weight of transplanted (■, □) and intact rats (●, ○). Body weight was followed for 4 weeks after VMH (●, ■), ○, □, Sham-operated. The increase in the lesioned rats without pancreatic transplants was statistically significant. The rats with pancreatic transplants and VMH lesions gained slightly, but not significantly more weight than the sham-transplanted animals. All data are presented as the mean $\pm$ s.e.m.

average of 319 g 4 weeks after the VMH lesions. The two groups of sham-operated rats (both with and without transplanted pancreatic tissue), showed a significantly smaller rise in weight than the VMH-lesioned rats with normal pancreatic tissue. There were no significant differences in the weight gain between VMH-transplanted rats and sham-operated animals. The Lee index, when the animals were killed, was used to measure fatness. It showed a significant increase in body fat in the control rats with VMH lesions, but no differences in body fat in the other groups, including the lesioned rats with transplants (Table 1). Food intake increased 71% in the lesioned rats with the normal pancreas but only 23% in the lesioned rats with transplanted tissue. The diurnal pattern of food intake was also measured during the third week after VMH operation. The ratio of food intake between 0900 and 1800, and between 1800 and 0900, was 3.3/14.5 and 3.1/14.3 for the two sham-lesioned groups. In the VMH-lesioned rats with normal pancreas, this ratio was 10.1/18.9. In the VMH-lesioned rats with transplants, the ratio was 6.0/14.9.

The results of the present experiment show that: removal of the pancreas from its usual neural influences markedly reduced the effect of ventromedial hypothalamic lesions on body weight and food intake; and that release of a humoral factor directly from the hypothalamus is not a sufficient

Table 1 Food intake and fatness of rats with transplanted pancreatic tissue, with or without hypothalamic lesions

Group	Animals	VMH	Operation pancreatic transplant	Food intake† (g d ⁻¹)	P	Lee index*	P
1	6	+	—	29.3 $\pm$ 0.8	<0.001	32.7 $\pm$ 0.36	<0.01
2	6	—	—	17.1 $\pm$ 0.4	<0.01	28.8 $\pm$ 0.18	N.S.
3	5	+	+	20.5 $\pm$ 0.5	<0.01	29.6 $\pm$ 0.17	N.S.
4	5	—	+	16.7 $\pm$ 0.4		29.2 $\pm$ 0.14	

*Lee index = $\frac{(\text{body weight (g)})^{1/3}}{\text{naso-anal length (mm)}}$; value at termination of experiment.

†Food intake was measured during the second week after VMH operation.

explanation for the high food intake and weight gain in rats with VMH lesions.

The vagus and sympathetic nerves both provide neural connections to the pancreas. The finding of gastric hypermotility and hyperacidity in rats with hypothalamic obesity suggests that the firing rate of the vagus nerve may be enhanced either directly or indirectly after VMH injury¹⁹. Further support for a role of the vagus nerve was provided by Powley and Opsahl who showed that vagotomy reversed the hypothalamic obesity¹⁶ and by the fact that stimulation of the vagus increases insulin secretion^{20,21}. The finding of a correlation between the level of acid in the stomach and the concentration of insulin in the serum of rats which had VMH lesions and varying degrees of vagotomy also suggest that the enhanced activity of the vagus nerve plays an important role in the syndrome of hypothalamic obesity¹⁸.

The sympathetic nerves are also known to modulate insulin secretion from the pancreas^{22,23}. Whether lesions in the ventromedial hypothalamus modify both components of the autonomic nervous system or only one remains to be established. What seems clearly demonstrated by the present experiment is that primary neural innervation of the pancreas plays a central role in the development of the increased food intake and obesity that follow ventromedial hypothalamic injury.

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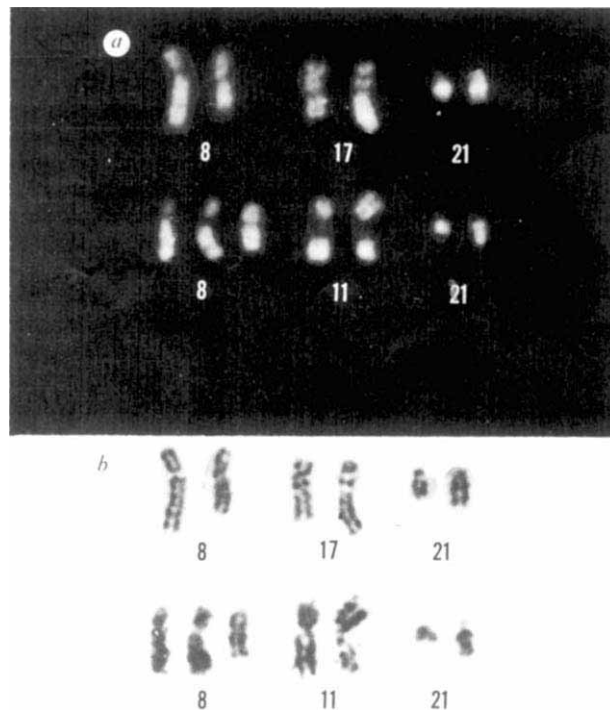
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relatively consistent translocations in several types of leukaemia and lymphoma lends credence to Boveri's hypothesis¹ that chromosomal alterations are among the fundamental changes that result in malignancy. For example, the Philadelphia (Ph¹) translocation² is observed in 85-90% of patients with chronic myelogenous leukaemia (CML), and the 8;21 translocation is observed in 10-15% of patients with acute myelocytic leukaemia (AML)^{3,4}. We report here that, when more complex structural changes occur, comparable patterns of rearrangements are found for both the 9;22 and the 8;21 translocations. This provides further support for Boveri's hypothesis.

The common rearrangement in AML involves a translocation of about one-third of the long arm of chromosome no. 8 to the end of no. 21 [t(8;21)(q22;q22)] (ref. 3). This rearrangement is often associated with loss of a sex chromosome, an X in female or a Y in male patients, which is otherwise a very rare occurrence in acute leukaemia. Whereas the original report³ and subsequent confirmations⁴ identified rearrangements involving only nos 8 and 21, we observed a variant translocation in a female patient with AML, in whom the translocation from no. 8 involved the end of the long arm of no. 17, and in whom there was an associated loss of an X chromosome (Fig. 1)⁵. Analysis with fluorescence revealed this abnormality in 22 of 26 cells (85%) obtained from the initial pretherapy sample and in 5 of 10 cells (50%) in a sample obtained 2 weeks later, while the patient was receiving chemotherapy.

A second female patient with a variant has been identified; the translocation from 8q involved the end of the short arm of no. 11 without loss of one X, but with the addition of one no. 8. In this patient, one no. 21 appeared larger than normal because of the presence of a narrow dull band of fluorescent material, presumably band 11p15 [47,XX,+8,t(8;11;21)(q22;p15;q22)] (Fig. 1). The complex

Fig. 1 Partial karyotype of cells from two patients. *a*, Stained with quinacrine; *b*, stained with Giemsa. Top row, chromosome nos 8, 17 and 21, showing the deletion of 8q22, transfer of this material to 17q23?, and the additional material on 21q presumably representing the end of 17q(q23→qter). Bottom row, chromosome nos 8, 11 and 21, showing the presence of two normal chromosomes no. 8 and the deletion of the third at 8q22 transfer of this material to 11p15, and the additional band on 21q presumably representing 11p15→pter.



Comparable complex rearrangements involving 8;21 and 9;22 translocations in leukaemia

FOR many years chromosomal abnormalities in tumours seemed to be so variable that it seemed most reasonable to view them as epiphenomena. But banding techniques have revealed non-random chromosomal abnormalities in several human and mammalian malignancies. The observation of

translocation was seen in 4 of 18 cells (22%) in the pre-treatment sample and in 13 of 14 cells (93%) in the sample obtained 10 d later.

Re-examination of the previous patient with the 8;17 translocation showed an analogous aberration of no. 21, compatible with a translocation from 17q (band 23?); the corrected karyotype should be 45,X,t(8;17;21)(q22;q23;q22). The break points in nos 8 and 21 in these two cases were similar to those in the standard 8;21 translocation.

The relevance of these observations to the role of chromosomal changes in leukaemia becomes apparent when one considers variant translocations in patients with Ph⁺ positive CML. In most of these patients, a portion of the long arm of no. 22 (Ph⁺ chromosome) is translocated to the end of the long arm of no. 9; this type of translocation was observed in 413 of 440 patients whose cells have been examined with banding⁶. Of the 27 cases with other rearrangements, 15 had translocations affecting three chromosomes; in each instance, two of the three chromosomes involved were nos 9 and 22, with the standard break points. Most of the remaining patients showed a translocation between no. 22 and some chromosome other than no. 9. Thus a parallel exists between the chromosomal changes in CML and in AML. In each case, two chromosomes are preferentially involved in a translocation; in some cases three chromosomes are affected, two of which are those involved in the typical translocation.

The mechanism producing such specific chromosomal rearrangements remains an enigma. Whether it is related to proximity in the nucleus or to homologous sequences of DNA, or whether it is the result of some selective advantage, is unknown. The observation of similar 'rules' governing two different translocations in two different types of leukaemia suggests that these changes are subject to precise, although as yet undetermined controls, and lends support to Boveri's hypothesis that chromosomal changes are among the fundamental alterations associated with malignancy.

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Derepression of *E. coli trp* operon on interfamilial transfer

THE P-group R factor RP4 originally isolated from *Pseudomonas aeruginosa* can be transferred to many Gram-negative bacteria¹⁻³. In spite of its large molecular weight, RP4 has only one site susceptible to each of *Eco*RI (ref. 4), *Hind*III (ref. 5) and *Bam*NI (data not shown) restriction endonucleases. We have constructed an RP4-*trp* plasmid consisting of RP4 DNA and the complete tryptophan operon of *E. coli* obtained from bacteriophage λ trpE-A₆₀₋₃ *in vitro*⁶. We reported that the tryptophan synthetase activity in the strain carrying RP4-*trp* plasmid was repressed by exogenous tryptophan⁷. Manson and Yanofsky have reported that the

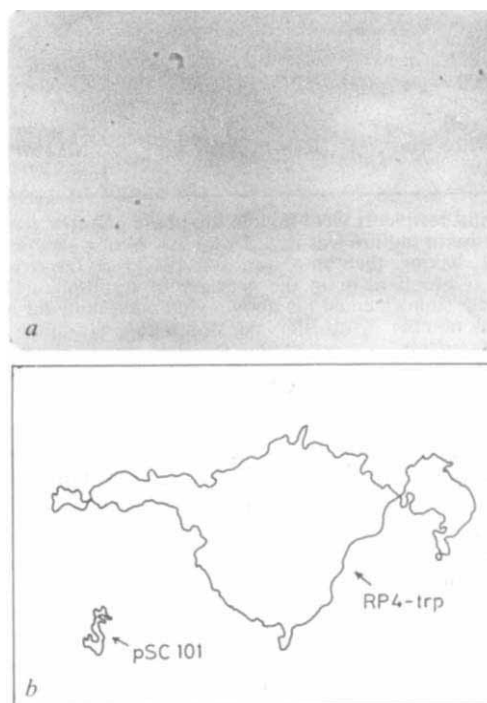


Fig. 1 Electron micrograph of RP4-*trp* DNA obtained from *P. aeruginosa* M12. pSC101 (molecular weight 5.8×10^6) was shown as internal standard. RP4-*trp* DNA was calculated to be of 48×10^6 molecular weight.

E. coli trp operon on the colVB plasmid was similarly regulated in other enteric species⁸. We show here that the RP4-*trp* plasmid in *E. coli* can be transferred by conjugation to *Pseudomonas aeruginosa* which belongs to a different family from *E. coli*, converting *Pseudomonas* Trp⁻ phenotype to Trp⁺. The levels of tryptophan-synthesising enzymes in *P. aeruginosa* carrying RP4-*trp* plasmid are much higher than those in the wild strain, and they are not controlled by the repression system in *P. aeruginosa* cells.

Table 1 shows that the transfer frequency of RP4-*trp* plasmid from *E. coli* cells to *P. aeruginosa* cells was lower by two orders of magnitude than that between *E. coli* r⁻km⁻ strains, whereas the transfer frequencies of RP4-*trp* from *E. coli* to *P. aeruginosa* for Trp⁺ and Carb^R markers are almost equal (Table 1), implying that the low frequency is due to the presence of a restriction systems or some other mechanisms in *P. aeruginosa* cells but not to the inactivity of *trp* operon of *E. coli* in *P. aeruginosa*. So far, all the transformants selected for resistance to carbenicillin were also tryptophan independent and vice versa.

Activities of two enzymes belonging to tryptophan operon, anthranilate synthetase (ASase) and the β subunit of tryptophan synthetase (TSase) were measured in crude extracts of cells grown in non-repressed or repressed condition (Table 2). The levels of both enzymes in the *P. aeruginosa* M12 strain (PAO subline) carrying RP4-*trp* plasmid were markedly elevated compared with those in a wild *P. aeruginosa* PAO strain which has chromosomally-located *trp* genes, and showed almost equal enzyme activities in both non-repressed and repressed conditions.

Calhoun *et al.*⁹ reported that in wild-type *P. aeruginosa*, the presence of exogenous L-tryptophan during growth in a minimal salts-glucose medium had no influence on the specific activities of ASase, 5-phosphorylribose 1-pyrophosphate phosphoribosyl transferase, N(5'-phosphoribosyl) anthranilate isomerase and indoleglycerol 3-phosphate synthetase in the cells, whereas their real repressibility by

Table 1 Transfer frequency of RP4-*trp* plasmid

Donor	Recipient	Selection	Transfer frequency
<i>E. coli</i> C600 <i>r⁻km⁻ktrp⁻</i> (RP4- <i>trp</i>)	<i>E. coli</i> C600 <i>r⁻km⁻ktrp⁻str^R</i>	Trp ⁺ Carb ^R	1.7×10^{-2} 1.3×10^{-2}
<i>E. coli</i> C600 <i>r⁻km⁻ktrp⁻</i> (RP4- <i>trp</i>)	<i>P. aeruginosa</i> M12 <i>str^R</i>	Trp ⁺ Carb ^R	1.8×10^{-4} 1.2×10^{-4}

Donors and recipients were middle log-phase cultures grown in nutrient broth supplemented with 0.4% KNO₃ without shaking at 37 °C. 0.5 ml of a donor culture was mixed with 2.5 ml of a recipient culture with 2.0 ml of fresh broth and this mixture was incubated at 37 °C for 2 h without shaking, then an aliquot was plated on the streptomycin (100 µg ml⁻¹) containing Vogel and Bonner's minimal medium in the absence of tryptophan, or in the presence of tryptophan (Trp, 50 µg ml⁻¹) and carbenicillin (Carb, 500 µg ml⁻¹) for transfer to *E. coli*. Appropriately supplemented (as above) glutamate minimal medium¹⁰ was used for transfer to *P. aeruginosa*. The frequency of transfer was calculated as number of transfers per donor cell. Strains used were *E. coli* C600 *r⁻km⁻ktrp⁻* (RP4-*trp*), restriction and modification minus *E. coli* C600 *leu⁻thr⁻thi⁻trp⁻* containing RP4-*trp*; *P. aeruginosa* M12 (ref. 10), *trp*.

exogenous tryptophan were revealed only in tryptophan auxotrophic mutants which caused the strict deprivation of intracellular tryptophan in depressed culture condition. In contrast the TSase activities in *P. aeruginosa* were much reduced in the presence of exogenous tryptophan and induced by their substrate indoleglycerolphosphate. Our data on PAO (wild type) strain are consistent with their observations, but a striking difference exists in the specific enzyme activities of strain M12, which has received the complete *E. coli* tryptophan operon in the form of RP4-*trp* plasmid DNA. Strain M12 carrying RP4-*trp* showed much higher levels of both ASase and TSase activity, and neither enzyme was repressed by exogenous tryptophan.

The amount of RP4-*trp* DNA in *P. aeruginosa* measured on a CsCl-ethidium bromide density gradient was almost equal to that of RP4 DNA in the same host strain (data not shown), indicating that RP4-*trp* was limited in number as RP4. This confirms our assumption that the expression of the *E. coli* tryptophan operon was out of the control of the *P. aeruginosa* repression system.

The molecular weight of RP4-*trp* in *P. aeruginosa* was 48×10^6 (Fig. 1), which was the sum of the RP4 DNA (38×10^6) and the tryptophan fragment (10.8×10^6) derived from λ trpE-A₆₀₋₃ DNA. The two bands, one corresponding to 10.8×10^6 and the other presumably to 38×10^6 daltons could be seen in agarose gel electrophoresis of EcoRI-digested RP4-*trp* DNA obtained from *P. aeruginosa* M12 cells (data not shown), showing that the complete *E. coli* RP4-*trp*⁷ was transferred to *P. aeruginosa*. Together with the transfer experiments this shows that the RP4-*trp* DNA has not been changed by deletion or insertion during conjugation.

These results imply that the *trp* repressor protein of *P. aeruginosa* cannot bind to the *trp* operator region of *E. coli* and so the *trp* gene products are expressed constitutively. The *P. aeruginosa* Trp phenotype has been converted to Trp⁺ by the effective transcription and translation of the *E. coli* *trp* operon by the *Pseudomonas* system.

Manson and Yanofsky discussed the suggestion that the

identical regulation of the *E. coli* *trp* operon in many of the Entero-bacteriaceae is proof of their common ancestry. The Family Pseudomonadaceae, however, seems to have diverged from the Family Enterobacteriaceae further back in evolution.

These experiments were carried out using precautions corresponding to the P3 containment level suggested by the US National Institutes of Health. *P. aeruginosa* and *E. coli* are natural hosts of the RP4 plasmid, and the fact that the *E. coli* *trp* operon is translated effectively in *P. aeruginosa* prove that the translation codes are identical in these two organisms suggests that possibly dangerous 'unknown' proteins would not be produced by this combination.

We thank Miss T. Koshikawa for technical assistance. We also thank Dr M. Kageyama of this institute for discussions and for supplying *P. aeruginosa* PAO1 and M12 strains.

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Table 2 Specific activities of tryptophan-synthesising enzymes in *P. aeruginosa* PAO1 wild type and M12 carrying RP4-*trp*

Strain	Trp	ASase	TSase β
PAO1	+	1.41	0.38
	-	1.53	2.17
M12 (RP4- <i>trp</i>)	+	6.59	19.0
	-	6.11	21.2

Cells were grown in glutamate minimal medium with or without tryptophan (100 µg ml⁻¹) and harvested in late exponential phase. The preparation of crude cell extracts and the assays for anthranilate synthetase and β subunit of tryptophan synthetase activities have been described⁸.

Correlation between the X-ray structure of melanostatin and its conformation in solution

THE establishment of correlations between solid-state (for example, X-ray) conformations and conformations in solution (monitored by spectroscopic methods such as nuclear magnetic resonance (NMR)) is essential for the understanding of structure-function relationships in biologically active molecules. The relative functional importance of static and dynamic

structures is of particular interest for peptide hormones which reach their site(s) of action on the receptor via a fluid medium. We describe here a comparative study of melanostatin (Pro-Leu-Gly-NH₂) which acts as a melanocyte stimulating hormone release-inhibiting factor¹.

Melanostatin was chosen for study because its X-ray structure is known², its minimum energy conformations have been computed³, and ¹H NMR studies in deuterated dimethylsulphoxide⁴ and in aqueous solution⁵ provide information about the time-averaged values of the dihedral angles in the backbone and side chains. We used ¹³C NMR spin-lattice relaxation times⁶ (*T*₁) of the proton-bearing carbons of melanostatin, in conjunction with a plausible theoretical model of molecular reorientation, to elicit dynamical information about the conformation in solution. The model for reorientational relaxation is stochastic rotational diffusion, with parameters optimised by a nonlinear least-square procedure^{7,8}. From these one can estimate both the overall molecular tumbling rate in solution, and the rates of internal motion about individual bonds. Thus the *T*₁ data facilitate study of the relative flexibilities of the various molecular fragments.

We first attempted to correlate the ¹³C NMR *T*₁ values obtained for melanostatin in aqueous solution with theoretical values calculated for the rigid X-ray structure. This rigid conformation was assumed to tumble about the three principal axes of its moment of inertia tensor with the optimal diffusion rate constants *D*_i. Even fully anisotropic (*D*₁ ≠ *D*₂ ≠ *D*₃) overall rotation of the rigid X-ray structure cannot account for all the observed *T*₁ values. This conclusion is unchanged even if the molecule is assumed to take on the unlikely fully extended conformation. Furthermore, the least-squares fit is not improved if the reorientation axes are chosen optimally rather than forced to coincide with the principal axes of the moment of inertia tensor. It was necessary to invoke internal motion for various molecular fragments in order to reproduce the observed *T*₁ values of melanostatin.

¹³C *T*₁ values were measured in aqueous solution (50 mg ml⁻¹) using the inversion-recovery technique⁹. Complete nuclear Overhauser enhancements (NOE) were obtained for all proton-bearing carbons¹⁰. Table 1 shows ¹³C *T*₁ values determined for Pro-Leu-Gly-NH₂ in which the prolyl residue is uncharged. Fig. 1 depicts molecular models of the folded and extended forms of the tripeptide we used in the calculation. The models are viewed along the C and B principal axes of the moment of

inertia tensor for the folded and extended forms, respectively. The moments of inertia were calculated from the Cartesian coordinates of all the atoms¹¹. The ORTEP thermal-ellipsoid plot programme for crystal structure illustration¹² was used to draw the figures. A nonlinear least-squares procedure^{7,8} was used to determine optimal sets of anisotropic rigid body rotational diffusion constants *D*_i, using experimentally obtained *T*₁ values and the computed direction cosines of the corresponding C-H vectors. C-H distances were assumed to be either 1.09 Å, or the actual values deduced from the X-ray data; the qualitative conclusions do not depend on the choice of the C-H distances. Table 1 lists the optimal effective correlation times *τ*_i (*τ*_i = 1/6*D*_i) for overall rigid anisotropic molecular reorientation about the principal axes of the moment of inertia tensor, as well as the *T*₁ values calculated with these correlation times. Results are shown both for the X-ray structure and the fully extended form.

When all proton-bearing carbons are included in the least-squares fitting, the *T*₁'s of the α-carbons are matched reasonably well (within ±40%). *T*₁ values for the CH₂ groups in the proline ring and for the CH₃ groups of the leucyl residue, however, were only within a factor of 2–3 of the experimental values. It is reasonable to ascribe these discrepancies to flexibility within the pyrrolidine ring of proline¹³ (probably puckering motion), and to rapid internal rotation of the CH₃ groups¹⁴. We repeated the calculations in the absence of these carbons. This led to *τ*_i values qualitatively the same as in the all-carbon case and which produced *T*₁ values for the α carbon of the prolyl, and the α, β, and γ carbons of the leucyl residue that were within the experimental uncertainties (±10%) of the measured *T*₁ values. Of special interest is the discrepancy between observed and calculated *T*₁ values for the glycyl residue. This is attributed to increased flexibility of this residue with respect to the remainder of the peptide backbone, a feature which is emerging as characteristic of glycyl residues⁷.

The overall molecular tumbling of the X-ray conformation is not markedly anisotropic, having effective correlation times of 5.9, 7.5 and 3.0 × 10⁻¹¹ s for rotation about the principal axes A, B and C of the moment of inertia tensor. Because the overall motion is nearly isotropic, displacement of the principal axes of the rotational diffusion tensor from corresponding axes of the inertia tensor would have little effect on calculated *T*₁. Calculations were repeated for a fully extended conformation in order to test the sensitivity of the calculated *T*₁ values to

Table 1 Least-squares fit of rotational correlation times to ¹³C *T*₁ values of melanostatin

Carbon atom	Observed <i>T</i> ₁ (s)	Calculated <i>T</i> ₁ (s)							
		X-ray conformation				Extended conformation			
Pro αCH	1.00	1.35*	0.99*	1.03*	0.96*	0.84*	0.89*	1.03*	0.95*
βCH ₂	0.88	0.56*	0.48*	0.46	0.42	1.03*	0.92*	0.46	0.43
γCH ₂	1.23	0.65*	0.44*	0.51	0.42	0.67*	0.69*	0.51	0.39
δCH ₂	1.00	0.63*	0.48*	0.50	0.39	0.83*	0.77*	0.50	0.44
Leu αCH	0.68	0.77*	0.89*	0.72*	0.75*	0.83*	0.87*	0.72*	0.94*
βCH ₃	0.43	0.48*	0.46*	0.42*	0.37*	0.62*	0.62*	0.42*	0.48*
γCH	0.90	1.26*	0.93*	1.01*	0.69*	0.83*	0.87*	1.01*	0.94*
δCH ₃	0.92	0.38*	0.29*	0.31	0.27	0.50*	0.50*	0.31	0.29
δ'CH ₃	0.92	0.40*	0.30*	0.32	0.27	0.52*	0.50*	0.32	0.30
Gly αCH ₂	0.63	0.56*	0.48*	0.46*	0.37*	0.60*	0.64*	0.45*	0.46*
Euler angles†									
α		(0)	115.0	(0)	77.0	(0)	-29.0	(0)	55.0
β		(0)	-76.0	(0)	-48.0	(0)	0.0	(0)	-31.0
γ		(0)	51.0	(0)	53.0	(0)	0.0	(0)	36.0
Optimal correlation times‡ (s)	<i>τ</i> _A	5.0 × 10 ⁻¹¹	6.8 × 10 ⁻¹¹	5.9 × 10 ⁻¹¹	1.2 × 10 ⁻¹⁰	7.2 × 10 ⁻¹⁰	3.9 × 10 ⁻¹¹	5.9 × 10 ⁻¹¹	6.9 × 10 ⁻¹¹
	<i>τ</i> _B	8.0 × 10 ⁻¹¹	5.4 × 10 ⁻¹¹	7.4 × 10 ⁻¹¹	4.9 × 10 ⁻¹¹	2.8 × 10 ⁻¹¹	8.1 × 10 ⁻¹¹	7.5 × 10 ⁻¹¹	7.5 × 10 ⁻¹¹
	<i>τ</i> _C	1.9 × 10 ⁻¹¹	3.8 × 10 ⁻¹¹	3.0 × 10 ⁻¹¹	3.6 × 10 ⁻¹¹	5.9 × 10 ⁻¹²	7.6 × 10 ⁻¹²	3.0 × 10 ⁻¹¹	3.0 × 10 ⁻¹¹

*Carbons which were included in least-squares fit.

†Euler angles characterising deviation between rotational diffusion and moment of inertia tensor axes.

‡*τ*_i = 1/6*D*_i, where *D*_i are rotational diffusion constants.

All C-H distances are 1.09 Å.

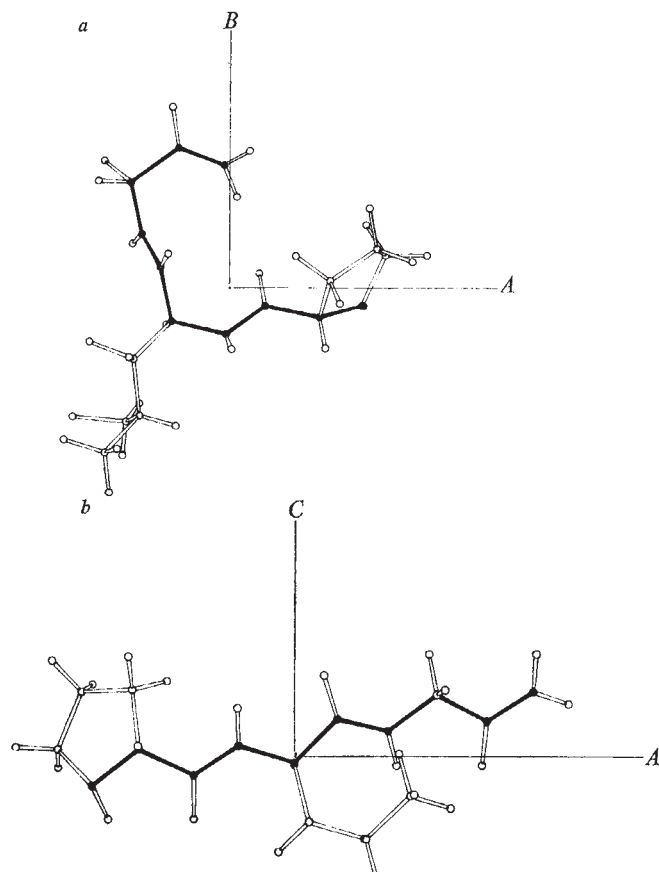


Fig. 1 Conformations of Pro-Leu-Gly-NH₂. Axes are drawn along principal axes of the moment of inertia tensor. *a*, Conformation determined from X-ray crystallography. Model viewed along the C axis. Moments of inertia (*I*) $I_A = 1,897.7$, $I_B = 2,174.4$, $I_C = 3,661.8$ a.m.u.Å² (1.00:1.15:1.93). *b*, Extended structure. Model viewed along the B axis. $I_A = 636.5$, $I_B = 3,571.4$, $I_C = 4,037.6$ a.m.u.Å² (1.00:5.61:6.34).

conformational differences. Even though the overall fitting errors are comparable for the two conformations, the optimal sets of τ_1 values are physically less reasonable for the extended form (in some instances spanning three orders of magnitude).

Having established that only internal flexibility can account for the observed T_1 values, we estimated optimal rates of internal rotation about individual C-C bonds. This was done both for the CH₃ groups and for the C _{α} (Leu)-C _{α} (Gly) pseudo-bond¹⁶ in the backbone. The values for the effective correlation times τ_A , τ_B , τ_C describing overall molecular reorientation of the X-ray conformation were the optimal values obtained fitting the backbone carbons only. Using an ellipsoid of rotation for the overall molecular shape, the effective correlation times we calculate for the CH₃ rotation ($\tau_{int} = 5 \times 10^{-12}$ s) and for rotation about the pseudo-bond ($\tau_{int} = 5.9 \times 10^{-11}$ s) are physically reasonable, further confirming the postulate of internal mobility. No attempt was made to estimate the rate and amplitude of puckering in the proline ring.

Correlating the X-ray structure with ¹³C NMR relaxation data has shown that in solution Pro-Leu-Gly-NH₂ is not rigid on the NMR time scale. The T_1 data seem to be good qualitative monitors of internal mobility in linear peptides, and when interpreted on the basis of simple theoretical models of rotational reorientation, can identify and locate flexibility within the molecule. The overall molecular shape of peptides the size of melanostatin (and up to molecular weight ~1,000) has minor influence on the calculated rates of internal rotation about individual C-C bonds¹⁵. Thus side chain-side chain interactions and their influence on the mobility of adjacent residues in

peptides and peptide hormones can be profitably studied using ¹³C NMR relaxation measurements in solution, without the need for precise information on the overall molecular shape. Such studies, coupled with experiments on the influence of solvents on T_1 (which probe changes in mobilities or structure due to the changing environment), with rotamer population data derived from spin-spin coupling measurements, with proton-proton relaxation results, and with predictions from conformational calculations, can provide consistent dynamical information about peptides in solution and may enhance our understanding of structure-function or conformation-function relationships in peptide hormones.

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Errata

In the article 'Mantle helium in the Red Sea brines' by J. E. Lupton, R. F. Weiss and H. Craig, *Nature* **266**, 244-246, the labels 714-G8 and Discovery in column 1 of Table 1 should be transposed.

In the article 'Direct demonstration of β -globin mRNA in homozygous Ferrara β_0 -thalassaemia patients, the author sequence should have read S. Ottolenghi, P. Comi, B. Giglioni, R. Williamson, C. Vullo, L. del Senno and F. Conconi. Figure 3 description line 2 should read Nuclear (a) and cytoplasmic (b) . . .

Corrigendum

In the article 'Punishment learning and self-mutilation in Lesch-Nyhan disease, *Nature* **265**, 461-463, sentence 1 of paragraph 2 should read 'Lesch-Nyhan disease is an X-linked recessive disease . . . '.

matters arising

The 17-d periodicity of Cygnus X-3

ARIEL V observations have indicated¹ a possible 16.75-d periodicity in the flux of Cygnus X-3. I report here that the primary data (from ref. 1) have been digitised and power-spectrum analysed; the results are shown in Fig. 1. (Analysis details available from the author.) The power spectrum shows a broad continuum of fluctuations, with an r.m.s. variation $\sim 40\%$ of the average flux for periods ≥ 3 d and a power law spectrum, $P(f) \propto f^{-1.5}$. This is not the spectrum expected from a shot-noise source².

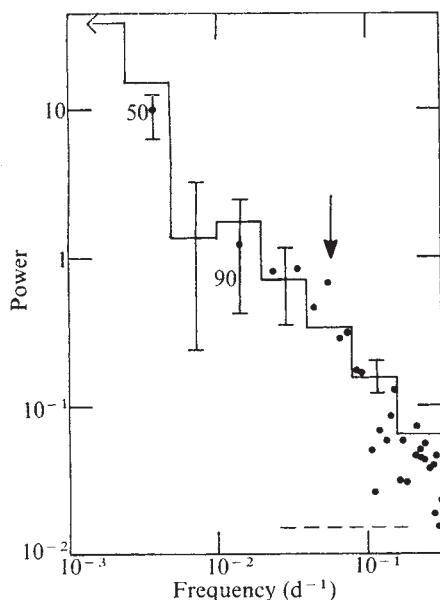


Fig. 1 Relative power spectrum of the flux of Cygnus X-3. Circular points are spectrum using FFT method (typical 50% and 90% confidence intervals are shown). The histogram gives spectrum using nested variance technique (90% confidence intervals shown). Dashed horizontal line represents noise level.

The arrow in Fig. 1 indicates a small peak in the power spectrum at the 16.75-d periodicity discussed in ref. 1. The significance of the peak is estimated from the excess power above the background fluctuation level (rather than above the Poisson noise level)². There is about 50% likelihood that there exists a 16.75-d periodicity. This periodicity, if real, accounts for

$\sim 10\%$ of the fluctuations and has an r.m.s. amplitude $\sim 4\%$ of the total flux.

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¹ Holt, S. S. *et al.* *Nature* **260**, 592–594 (1976).

² Terrell, N. J. *Astrophys. J.* **174**, L35–L41 (1972).

HOLT REPLIES—Owens implies that the ~ 17 -d periodicity reported in ref. 1 may be artefactual, in view of the broad continuum of fluctuations evident in the raw data. We have no quarrel with such a qualification; indeed, ref. 1 explicitly pointed out that the high degree of source variability, variable gaps in coverage, and no explicit correction for the known 4.8-h source modulation could be expected to result in artefactual frequency components in the data analysis.

The ~ 17 -d effect was not, therefore, reported solely on the basis of it being the most significant (statistically) period in the search we performed on the Ariel V All-Sky Monitor data. We felt that the apparent presence of the same effect in the Ariel V Sky Survey Experimental data, which were corrected for 4.8-h variations and which were obtained during extended gaps in the All-Sky Monitor exposure (so that the two sets of data were completely independent), was sufficient justification for alerting the scientific community to the possibility of its reality. We regret that the quality of our data cannot support a stronger statistical argument for the presence (or absence) of a persistent ~ 17 -d modulation of the variable Cyg X-3 intensity.

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No new limit on size distribution of γ -ray bursts

Carter *et al.*¹ derived an upper limit to the (balloon) intensity of small γ -ray bursts at ≈ 100 below the extrapolated known size spectrum, and concluded that γ -ray bursts are of galactic origin. But we claim, for the following reasons, that their results are entirely consistent with the

-1.5 index power-law extrapolation. There is, therefore, no conclusion regarding the nature or the origin of γ -ray bursts to be drawn from their measurements.

(1) Their selection criterion for candidate events was that of three successive 0.6-s increases in the γ -ray count rate. A study of all known bursts (data kindly supplied by R. W. Klebesadel) shows that this requirement ignores 75% of events due to their widely varying temporal nature.

(2) The total energy sought in 1.8-s does not represent the entire energy that would be found, for the same reason. The missing energy due to fluctuations is incorporated by reassigning the event size by a factor of ≈ 2 .

(3) Observed γ -ray burst size spectra have been published^{2,3} with the measured flux of each known event multiplied by 1.4 to 2, to include the emission below the satellite energy threshold, knowing the typical spectra^{4–6}. Comparison data must normalise equivalently.

(4) The authors knowingly employed a 1-s.d. upper limit¹. Small-number statistics demand the usual confidence limit of 95%, raising their upper limit by three.

(5) The observed fraction of the sky was apparently taken to be 0.5, ignoring atmospheric absorption at large zenith angles which would give an unobscured sky fraction of 0.25–0.3. This point is incorporated within the following considerations.

(6) The response of a horizontal, flat detector must distort the measurement of the burst size spectrum, even from an isotropic source distribution. For a totally absorbing detector it can be shown⁷ that the average burst size $\bar{S}$ that contributes to the smallest events of apparent size $Z = S \cos \theta$, given an intrinsic spectrum $N(S) dS = kS^{-\gamma}$, is

$$\bar{S} = Z [(\gamma-1)/(\gamma-2)]$$

$$\times [(1 - \cos^{(\gamma-2)} \theta_0)/(1 - \cos^{(\gamma-1)} \theta_0)], \quad (2)$$

with θ_0 the maximum equivalent unobscured zenith angle θ . Using their published detector characteristics¹, we find a required vertical shift of 2.2 and a horizontal shift of 1.3 on the size spectrum, including point 5.

The total combined effect is that the upper limit rederived from the data of Carter *et al.*¹ is raised up by two orders of magnitude, entirely consistent with the -1.5 index power-law extrapolation

of the known size spectrum (Fig. 1). In fact, it is exactly an analogous threshold effect of lack of observation which depresses the Vela size spectrum low end by up to three orders of magnitude.

Even if (on the basis of no single-event observation) an upper limit below the

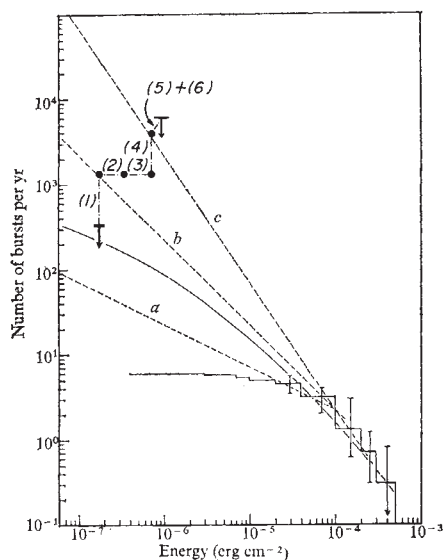


Fig. 1. The γ -ray burst results of Carter *et al.*¹, adjusted by six factors, numbered accordingly. Compare with Fig. 1 of ref. 1.

—1.5 index extrapolation were found, this alone would not prove either the size spectrum model or the origin hypothesis suggested¹. Such a result would imply only that the source distribution is not infinite in extent, assuming that the average absolute magnitude of emitters is independent of distance.

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⁶ Cline, T. L. & Desai, U. D. *Astrophys. J. Lett.* **196**, L43–L46 (1975).

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CARTER ET AL. REPLY—Cline and Schmidt¹ have presented a series of subjective arguments in an effort to show that our earlier reported upper limit to the rate of γ -ray bursts² can be made to conform with a hypothetical number-size spectrum with an index of $-3/2$. We believe that they have become too attached to this hypothesis. In fact, the data from the Vela satellite is equally consistent with an index of -2 , although this does not have the same cosmological attraction. If the power-law index were $-3/2$ then a detector with an energy of 10^{-7} erg should record a burst approximately every 2 h or so. No such evidence exists.

Our criterion for the recognition of γ -ray bursts was that the counting rate in each of three consecutive, and independent, measurements should exceed the background by 3σ . Unless one has a coincidence in a second, remote, sensor it would seem imprudent to claim excesses in a single measurement interval to be a genuine γ -ray burst. There is evidence of some poorly understood events in which anomalous increases arise in a single resolution element as well as effects which lead to the occasional saturation of a complete telemetry frame^{3,4}. Since the basic resolution time in our particular experiment was 0.6 s, an intrinsic limit of 1.8 s is set in our burst search. Although our main data analysis was confined to the above selection criterion, we did in fact search for possible shorter events. In this case, however, we required a coincidence in the counting rate from at least two of the differential energy channels. No evidence for γ -ray bursts was detected using this criterion either.

We had not discussed the rationale of our selection criterion nor the details of our analysis methods, in our original brief contribution since they are fairly standard procedures.

In the following sections we comment on the numbered points raised by Cline *et al.*

(1) From the existing published data^{5,6} it may be seen that the typical size for a γ -ray burst is 3–5 s and the first peak lasts ~ 2 s. The temporal variations seem to be of the same magnitude as the basic time resolution of the particular experiment. Our selection criterion, therefore, will be met by a substantial majority of these events. We will, admittedly, lose those events having a duration ≤ 1 s but we estimate this loss to be about 20% of the total.

(2) The limit shown in our figure corresponds to the selection criterion outlined above. We could have set a lower energy limit had we considered only longer bursts. But, since the typical length of γ -ray bursts is longer than our measurement interval and since the average intensity represents the first moment of the generating function, the upper limit deduced on this simple average basis is an adequate representation of the burst energy.

(3) The correction factor suggested here seems rather naive. First, there is no experimental evidence that the spectra of all bursts extend below 100 keV. From a comparison of the OGO and Vela results we estimate that only 60% of the events would meet this criterion⁷. Second, if the burst spectrum did, in each case, extend below 100 keV, the correction factor for the missing energy would be a function of the particular experiment. The use of a constant factor as suggested by Cline and Schmidt is absurd. The correction factor in our case was estimated to be 1.3.

(4) This point was adequately discussed in our text which we had expected to have

been regarded as an integral part of our presentation.

(5) When atmospheric effects, including multiple-Compton scattering had been taken into account we estimated that the effective field of view of our detector was $\sim 1.5\pi$ sr.

(6) The comments raised in this section have been discussed in the past in the context of cosmic-ray physics. Deductions from the mathematical treatment suggested by them is unwarranted in the absence of any established power-law index. The expression suggested by Cline and Schmidt is clearly erroneous since the value $\bar{S}/Z$ can be seen to be independent of the zenith angle for $\gamma = 3/2$. The expected number of bursts with a detector floating in the atmosphere can be written as

$$N_B = \sum_i w_i N(E_i)$$

where w_i is the solid angle and E_i the average threshold energy in the i th element. The expression can be solved to the required degree of accuracy with a knowledge of $N(E)$, the integral size spectrum of γ -ray bursts which is as yet unknown. Alternatively, the correction may be evaluated approximately, in a more practical way, independent of the size spectrum. For a given detector the energy deposited by a γ -ray burst must lie between E and $3E$ for zenith angles ranging between $\theta = 0$ and $\theta = 75^\circ$. This is due to a decrease in the effective area by a cosine factor. The detection efficiency at large zenith angles, however, increases due to increased path length in Na I by $\sec \theta$. Therefore the detector can be regarded as being less sensitive by a factor of about two. Such a consideration will make our earlier results an absolute upper limit for bursts with energy greater than 5×10^{-7} erg.

We conclude that the second-order refinements discussed above can, at most, contribute a factor of about two, both in burst energy and in burst rate. Cline and Schmidt are entitled to make their own assessment of our results but we maintain that these corrections do not materially change our conclusions and that, at this stage, we see no compelling reason to reconcile our results with their hypothesis.

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¹ Cline, T. & Schmidt, W. K. H. *Nature* **266**, 749–750 (1977).

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reviews

Nutrition and the developing brain

John Dobbing

Malnutrition and Intellectual Development. Edited by J. D. Lloyd-Still. Pp. 194. (MTP: Lancaster, 1976.) £8.95.

A SMALL epidemic of recent books on or around this topic imposes a special need to justify the addition of any new one to the bookshelves. Dr Lloyd-Still's is an edited volume of six reviews or essays, dealing in turn with: effects of undernutrition on the growth of the physical brain and on "mental competence"; techniques of psychological testing in this context; some studies of the subsequent physical and intellectual development of children inevitably malnourished in the course of certain clinical conditions in affluent society compared with eleven major studies from the underprivileged world; and finally the "social ecology" of malnutrition in childhood. It is nicely produced, and there is certainly enough excellence to justify its place alongside other recent books (for review, see *Nature*, 262, 521, 1976).

After a very thoughtful introductory chapter by the editor in which he gives a very balanced description of the whole subject, there is a disappointing second chapter by Peter Chase on the physical effects of undernutrition on the growing brain. I think my dissatisfaction with it largely derives from Chase's total lack of humility before the amazing complexity of the developing brain. Where the rest of us use curves of brain weight, cell number, myelin lipid and so forth as crude indicators of the timing of developmental events so as to identify hypothesised periods of enhanced vulnerability. Chase seems to think of such parameters as of specific significance in themselves. They are, of course, merely the things we can conveniently measure. Some of his graphs of their accumulation in whole brain are misleadingly wrong in places. And who is interested in whole brain quantities anyway, except in the limited sense mentioned above?

The third chapter by epidemiologists Zena Stein and Mervyn Susser draws heavily on their fascinating study of the effects on fetal growth and 19-yr-old achievement following the Dutch wartime famine during the winter of 1944-45. This is a beautifully

written, distilled account of their findings, cleverly described in the setting of many other epidemiological studies, including some in which there is experimental nutritional intervention. The book deserves to be bought for this chapter alone.

The Hurwitz chapter on psychological testing in studies of malnutrition is very useful in a different way. Assuming his descriptions of the test methodology are reliable (and I cannot judge that), I was most impressed with his account of the limitations of such tests in the present context. The problems of cross-cultural validity together with the difficulties of drawing "growth-curves" against age in longitudinal studies, seem even more formidable than one had imagined, to say nothing of the hazards in using infant tests as predictors of long term performance.

Lloyd-Still returns in Chapter 6 to discuss "Clinical Studies", by which he means direct studies on children. His tabulated condensation of 13 major studies includes 11 of socioeconomic or cultural malnutrition and two in which malnutrition was secondary to clinical

conditions in our own privileged communities. The breadth of his discussion is impressive and partly derives from his conspicuously profound experience as a children's doctor. One day, however, we shall have to abandon discussion of some of the earliest field studies since it is now too easy and somewhat redundant to criticise them. Their place is in historical introductions to theses.

The last chapter on the social ecology of childhood malnutrition unfortunately returns to the rather lower standard of the second. It may well be true that the "Soviet Union, which was able to purchase . . . grain with devalued dollars at prices subsidised by the United States Government, realised further profit, both economic and political, by selling, lending and granting of American grain to other countries"; but such statements are below the generally very high standards of objectivity in the remainder of this book. □

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Electrons in liquid ammonia

Electrons in Liquid Ammonia. By J. C. Thompson. Pp. xii+297. (Clarendon: Oxford; Oxford University: London, 1976.) £14.50.

THIS book is a gold mine of information for anyone working in any area of electrons in fluids. It is written by a person who has contributed to all of the many areas represented in this monograph. Professor Thompson has not only collected all of the major experimental and theoretical work on the subject but has presented it in a very critical but very fair manner. After reading this book everyone should have a better feeling for our present state of understanding as well as the remaining problems.

The major topics include "metal-ammonia solutions as liquid metals", "metal-ammonia solutions as electrolytes", "the metal-nonmetal transition", "liquid-liquid phase separations", "solutions of alkaline earth and rare Earth metals", "solid metal-ammonia compounds", and "solutions in other

solvents". Each chapter contains material which will prove useful to even the most well informed reader on the present status of each topic. The presentations are remarkably up to date and inclusive.

The strongest single point of this book is its emphasis on those areas in which our understanding of experimental data is very incomplete. In this regard one might mention spin pairing and the "metal-nonmetal" or conductivity transition. In these cases the author has made a special effort to quote all of the essential experimental facts as well as to make the strongest possible case for all of the alternative theoretical models (pointing out in addition that all fail on some other points).

This book is so vital that any researcher in any related field would be negligent if this book were not actively used as part of his routine research. **Neil R. Kestner**

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Human immunology

Immunology of Human Reproduction. Edited by J. S. Scott and W. R. Jones. Pp. xviii+476. (Academic: London; Grune and Stratton: New York, 1976.) £15.

THIS is a fascinating book for all those who have an interest in immunology and development. The book begins with a glossary and a primer of immunology that has freed later chapters from the need to define and explain. This introductory section is oversimplified in places and occasionally patronising, but these faults are outweighed by the good it does in summarising and ordering a field overgrown with observations and special terminology.

Although no formal break is made, I would divide the remaining chapters into two sections: chapters 2-6 dealing with basic aspects of immunology in development, and drawing on both clinical material and animal, model, experiments; and chapters 7-13, dealing largely with clinical aspects of human immunology and development. The chapters are of varied length, quality and distance from the stated topic of the book, but they all elaborate their topics in considerable detail, and it is this detail that is the book's strength.

The authors themselves are often moved by the complexities and uncertainties of the topics, to use phrases like "the tip of the iceberg of confusion" or to make statements such as "existing knowledge concerning the role of immunological factors in gestosis is fragmentary . . ." or "the picture . . . as in so many areas of reproductive immunology is confused . . ." This confusion is, however, the result of contradictory or insufficient clinical and experimental observations, and by detailing these the authors have done a great service, allowing others to speculate on, and experiment over, the data presented here.

The fields of immunology and reproduction are connected at many points. Chapter 2, by M. H. Johnson, makes a connection between the two by discussing the stages of early mammalian development (exemplified by the mouse embryo) and some ways in which immunological techniques may be used to characterise these stages. In this chapter the problem is raised of the maternal immune response to antigens of the embryo, either to alloantigens, or to stage-specific antigens. This problem, still unsolved, is reiterated in later chapters, notably that by Billington on the immunology of trophoblast, and in a chapter by Medenhall, which considers all aspects of maternal-foetal immunology, transfers of maternal im-

munoglobulins and cells, and the problem of the foetal allograft. A further comment on the problem is made by Gusdon, in a chapter on the effects of pregnancy on all maternal immune responses. The first section closes with a chapter by W. Jones on the phylogeny and ontogeny of the immune response. This chapter considers development of foetal immune responses in its own right. It is perhaps too broad and contains a few notable factual errors (the mouse is assigned a 30-d, not a 20-d gestation period), but the section on the maturation of the immune responses of the human foetus is thorough, including the immunological aspects of breast feeding, and quite interesting.

In the second section we are given extended treatments of particular topics. Some, such as that of chapter 7 on the consequences of maternal infection for the foetus, cut across the divisions set up in the earlier chapters. Others, such as a chapter on the effect of pregnancy on immunological diseases of the mother, analyse a limited topic within the larger one already set. Maternal-foetal immunological interactions are prominent in Rh disease, and this topic receives full treatment in a chapter which emphasises clinical aspects of the disease, although failing to discuss the molecular aspects of Rh antigens and of the transfer of Rh antibodies across the placenta. Gestosis

(eclampsia/preclampsia), a condition involving the immune response in some obscure manner is also given a chapter of its own. If we are not convinced at the end of this chapter that the condition is due to immune responses, neither are we put off further exploration of the problem. Similarly, the role of the immune system and of cell surface antigens is unclear in cases of trophoblastic neoplasms. Again, the question cannot be answered but it is well set out and elaborated. Other chapters cover non-gestational reproductive tract neoplasms, and immunological aspects of infertility as well as the prospects for immunology in the control of fertility. All of the chapters carry long lists of references: the average is about 130; and one chapter, that by Edwards on immunology and fertility control contains 390.

The immunology of reproduction is a vast subject and, as will be seen from the individual subjects mentioned, may be taken in many senses. It would be too much to expect a consistent exposition of the subject; indeed, such an exposition would certainly be highly biased, if not false. The opposite approach taken here, if it occasionally daunts the authors, stimulates their readers.

Michael Edidin

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Volcanic picture book

Volcanoes and Impact Craters on the Moon and Mars. Pp. 463. By P. Leonardi. (Elsevier Scientific: Amsterdam and New York, 1976.) Dfl.166; \$59.75.

AT a first glance this book is very impressive; it is beautifully presented and contains large numbers of high quality pictures, both in colour and in black-and-white. For a subject which relies much on interpretation of photographs taken of other planets, this is highly commendable. The author has not only reproduced the standard NASA and Soviet pictures taken from spacecraft but has also included many extremely interesting pictures of geological phenomena on Earth.

Although the book was originally written in Italian it has generally speaking been well translated into English and reads easily. The author has obviously read widely around this subject and there can be few planetary scientists who will be disappointed at not finding their name in the index.

In view of these comments the reviewer would have liked to have recommended this book. But although pictorially the book is very much up-to-date (even containing Viking pictures), many of the ideas expressed in the text are reiterations of ideas current among some scientists in this field more than ten years ago, before spacecraft exploration of the Moon and planets. Much of the book is devoted to the old argument of impact as against volcanic craters on the Moon, and although the author presents the 'impactists' case fairly, his conclusions lie well within the 'volcanic' camp and would not be accepted by most planetary workers who have studied the evidence obtained during the past ten years.

Sadly, although recommended for its presentation and picture quality, this book will be of little interest to scientists in the field and can only be recommended to students for the historical interest of the text.

J. E. Guest

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Membrane enzymes

The Enzymes of Biological Membranes. Vol. 1: Physical and Chemical Techniques. Pp. xiii+257. £10.50; \$20. Vol. 2: Biosynthesis of Cell Components. Pp. xvii+654. £28; \$55. Vol. 3: Membrane Transport. Pp. xv+459. £21; \$39. Vol. 4: Electron Transport Systems and Receptors. Pp. xv+431. £20; \$37. Edited by A. Martonosi. (Wiley: London, 1976.) (US edition published by Plenum: New York, at slightly different prices.)

THESE volumes form the first four of a series which sets out to collect together and evaluate information on membrane enzymes. Most of the information is concerned with the relationship of enzymes to their membrane, and with their involvement in membrane phenomena. Very detailed information on the structure of each enzyme is usually lacking, since the purification and structural analyses of most membrane enzymes have not advanced as far as for their soluble counterparts.

Some membrane enzymes are dealt with singly, others appear as part of enzyme systems. It is clear from the volume titles that the word 'enzyme' has been interpreted very loosely. Thus, in addition to proteins with clear enzymic activity, the coverage includes binding

proteins of various persuasions, transport components without enzymic activity, and light-trapping systems; in short, membrane proteins with clearly documented biological function. This is a reasonable extension in the context of an attempt to provide an insight as to how membranes function. Very few important 'enzymes' have been omitted.

Each volume is a multi-author effort; the cast-list is impressive and most authors do their subject (and themselves) justice. The coverage given to different 'enzymes' varies; in some cases this is an overall view of the 'enzyme' and its relationship to the membrane, whereas in other chapters the emphasis is more firmly on recent developments. On the whole, most contributors reflect the state of knowledge in each field but occasionally reveal a personal bias which may limit the usefulness of their chapter.

In the first volume the uses of various techniques are discussed in establishing the general fluidity of the membrane lipid layer, in demonstrating a collar of lipid around the inserted portions of some proteins, and in interpreting the response of some enzymatic activities to temperature change; all of these discussions use suitable examples. Much of the same work is, however, discussed again in other volumes in relation to the properties of the individual enzymes used as the examples

in volume 1. This excessive overlap could have been avoided, as could the length of those contributions taking over 30 pages to discuss a single 'enzyme'.

Volume 4 is a very artificial assembly; the few chapters on receptors, with the exception of that on rhodopsin, have little in common with those on electron transport systems. The receptor chapters would have been better separated off into a further small volume or would have associated better with the transport components. Such considerations are clearly of importance to purchasers of individual volumes but of less importance when considering purchase of the series for a library.

To have such a convenient and comprehensive source of material on membrane enzymes will be a considerable asset in both teaching and research. The series is clearly one for library purchase since it is too comprehensive and expensive for individual subscription. Each volume deals with a coherent group of topics (with the artificial addition of the receptor section to volume 4); although expensive, they are therefore more attractive for single volume purchase than many serial publications.

Roger Coleman

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Disease resistance in plants

Defence Mechanisms of Plants. By B. J. Deverall. Pp. 110. (Cambridge University: Cambridge, London and New York, 1977.) £5.50.

THROUGHOUT their lives plants are exposed to infection by many parasitic microorganisms. Yet infection often fails and the plants remain healthy. Professor Deverall's excellent book is concerned with the processes by which plants perceive the parasite, and occasionally permit but usually discourage its further progress.

Professor Deverall does not attempt an extensive account of the subject but rather chooses to present a selective personal view of recent research pertaining to the processes of resistance to disease. Emphasis is placed on events which occur after a plant has been infected and covers cytological changes, the production of antimicrobial compounds (phytoalexins), induced resistance and the mediation of host-parasite specificity. Each chapter contains a summary of the facts, which is well supported by reference to original and review papers, an assessment of their significance or otherwise, an indication of the problems remaining, and in some cases how they may

be solved. Few significant errors or omissions have been noticed although the promise to expand the concept of infection type to all host-parasite interactions is rarely fulfilled.

This book is extremely timely in that it appears alongside several other publications, which although containing more detailed information often fail to analyse it critically. In this respect, Deverall, rather than merely providing a list of phytoalexins, presents a welcome evaluation of the evidence for their rôle in resistance and the mechanisms of their induction. The close association between cell death and phytoalexin synthesis rightly receives much emphasis, but his conclusion that phytoalexins are synthesised in living cells may be somewhat premature.

Professor Deverall states that he envisages his readers to be research workers and university lecturers, and their advanced students. The book can be recommended as essential reading for such people. It will convey the progress achieved by and the challenges remaining for physiological plant pathologists.

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Atmospheric chemistry

Atmospheric Chemistry. By J. Heicklen. Pp. xiv+406. (Academic: New York and London, 1976.) \$38; £27.

In view of the rapid expansion in knowledge of the chemistry of the Earth's atmosphere in recent years, publication of a new volume on this topic is timely. *Atmospheric Chemistry* by Julian Heicklen, however, does not in any way achieve the standard of information collection, dissemination and presentation in the two notable publications on this topic in the early 1960s: Leighton's *Photochemistry of Air Pollution* and Junge's *Air Chemistry and Radioactivity*.

The reason for this failure mainly arises from the authors attempt to cover too much ground; indeed some of the topics discussed—such as the kinetics and mechanism of hydrocarbon combustion, the detailed effects of urban pollutants on plants and animals, and pollution control methods—are inappropriate to the field encompassed by the title. On the other hand there is inadequate coverage of the basic large-scale and local meteorological factors determining the transport mechanisms that are so important in defining the reactor in which the chemical reactions take place.

In addition, the overall emphasis is very much towards photochemistry. Although it is true that the absorption of solar radiation is the primary driving force for chemical reaction in the atmosphere, the chemical interactions of trace gases with precipitation elements and the wash-out and rain out processes have an important part to play in the overall atmospheric cycles, and these are hardly discussed at all. This lack of balance detracts from the overall usefulness of the work in presenting an overview of the science of atmospheric chemistry.

The author must be credited, however, with the collection of a large amount of photochemical and kinetic information on the chemical reactions which may occur in the atmosphere. In the chapters on chemistry of the upper atmosphere and on photochemical smog, simple model calculations are developed to demonstrate how the trace gas composition in each particular atmospheric region can be simulated using the chemical kinetic information. This is basically a useful presentation, but unfortunately the arguments tend to become too complex and difficult to follow. Also, the uncertainties in applying the results to real atmospheric situations are not emphasised. For example, in the discussion of a model photochemical smog

system, the reader is left with the impression that ozone concentration in sunlit exhaust-polluted atmospheres are governed solely by the photochemical reactions. The important and often dominant role of meteorology, in determining ozone concentrations is not mentioned.

The lack of emphasis on precipitation chemistry is very apparent in the chapter dealing with SO_2 chemistry. A comprehensive 10-page summary is given of laboratory data on SO_2 photochemistry, a process which is widely accepted as being of negligible importance in the atmospheric chemistry of SO_2 . The droplet-phase oxidation of SO_2 is, on the other hand, dealt with in a cursory fashion with no reference to some of the early classic work carried out on this important system.

In addition to the above mentioned chapters, there is a concise description of the chemistry of the ionosphere, a long chapter on atmospheric pollutants, which contains very little atmospheric chemistry and a lot of useless information on concentrations in US

cities and deleterious effects, together with a short but not very illuminating chapter on aerosol chemistry. A chapter entitled reactions of O_3 and singlet O_2 also contains a detailed discussion of NO_2 photolysis.

There are some misconceptions and inaccuracies which are unsatisfactory for a book of this kind. For example: it is stated that "The troposphere is a relatively quiescent region (of the atmosphere) where relatively little chemistry occurs . . . The global atmosphere chemical cycles can be summarised as mainly oxidation occurring in the stratosphere . . .". This statement is manifestly untrue. In fact, nearly all of the gaseous material emitted into the atmosphere from the Earth's surface fails to penetrate the tropopause. It is oxidised or otherwise scavenged in the troposphere where 80% of the atmospheric mass resides.

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Ion cyclotron resonance spectrometry

Ion Cyclotron Resonance Spectrometry. By T. A. Lehman and M. M. Bursey. Pp. xi+230. (Wiley-Interscience: New York and London, 1976.) £15.95; \$27.30.

ION CYCLOTRON RESONANCE (ICR) spectrometry has been widely used during the past 10 years for the study of the chemistry of ions in the gas phase. Although it has found many applications in the field of chemical physics, it has been used increasingly in studies of the structure and reactivity of organic ions and in the elucidation of reaction mechanisms which parallel those observed in solution. It is on the latter group of applications that this volume concentrates, and by far the longest chapter in the book is devoted to a discussion of such topics as gas-phase acids and bases, nucleophilic and electrophilic substitution reactions, and structures of ions. It is written from the viewpoint of a physical/organic chemist and a number of interesting comparisons are drawn with results obtained from studies of solution kinetics.

This illustrates one of the major problems in writing a book on a particular experimental technique: the subject of gas-phase ion chemistry is much bigger than ICR spectrometry and by confining themselves largely to examples based on ICR studies, it can be argued that the authors present an incomplete and selective view of the field. For example, results obtained from high pressure mass spectro-

metry or by flowing afterglow and flowing after-drift methods have proved of considerable interest; and although comparisons are drawn between these results and those obtained by ICR spectrometry, discussion of them is necessarily brief.

The first two chapters of the book provide a very readable introduction to the technique in which the reader is encouraged to explore the possibilities of the technique without worrying too much about the finer points of its theory of operation. The chapter on reaction mechanisms is followed by a discussion of theoretical aspects of power absorption, linewidths and extraction of rate data together with a brief review of current theories of ion molecule reactions at near thermal energies. The final chapter briefly describes various applications of ICR spectrometry in the field of chemical physics. The book concludes with an extensive bibliography and two appendices.

The book provides a useful introduction to ICR spectrometry and to physical/organic aspects of gas-phase ion chemistry but the chemical physicist will find little which is not adequately covered in review articles. The problem with any book on a particular technique is that it is necessarily limited in its scope; and although the reader will know quite a lot about ICR spectrometry, if he gets through this book, he will not be in a position to assess its advantages and disadvantages relative to other techniques used in the study of gas-phase ions.

K. R. Jennings

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obituary

Sir Gerard Thornton

MICROBIOLOGISTS, especially those who had the good fortune to work with him, will have heard with sadness of the death of Sir Gerard Thornton on 6 February at his home in St. Albans at the age of 85. He is survived by his widow, Gerda, who is Danish, and by his son Peter who is Keeper of Woodwork and Furniture at the Victoria and Albert Museum.

He will be remembered for his many original and important studies on soil microbes, made in the course of a long career spent almost wholly at Rothamsted Experimental Station, Harpenden. He was educated at Radley and at New College Oxford and joined Rothamsted shortly after the end of the Great War where he had served as a pilot in the Royal Flying Corps.

In 1919, soil microbiology was a very rudimentary science, and Thornton's early work was much concerned with the devising of techniques for isolating, identifying and counting various kinds of soil bacteria and in promoting parallel studies by others on soil fungi, protozoa and other groups. With his friend the late R. A. Fisher he pioneered the application of statistics to the problems of enumerating bacteria in soil. At this time he was also in contact with the great European soil microbiologists—Beijerinck, Winogradsky, Kluver and later with Waksman. He had a special interest in the microbial breakdown of aromatic disinfectants in soil, and made a collection of bacteria able to utilise cresols, phenols and naphthalene as sole carbon sources and elucidated some aspects of their physiology. This work was later to become specially relevant to the discovery, which he shared with others, of the selective hormone herbicides (chlorinated phenoxyacids), first published in *Nature* (155, 498; 1945).

His greatest influence, however, was through his distinguished research on biological nitrogen fixation, especially by root-nodulated leguminous plants. His detailed investigation of their microbiology, structure and physiology laid the foundation for nearly all later work and led to practical applications in UK agriculture. His work established the 'bacteroid' as the nitrogen fixing site in the nodule and he described in detail the features of ineffective, non-fixing nodules. With his Rothamsted colleagues he was the first to use sero-

logical methods for identifying rhizobia and was associated with early work on bacteriophage and with studies on ecology of rhizobia. Thornton was also the first to investigate effects of competition between strains in the soil, a matter later shown to be important in the development of efficient 'inoculants' for leguminous crops. Since his retirement in 1957 he continued to show the greatest interest in nitrogen fixation and in the striking advances made world-wide in its study during the last decade, stimulated by the International Biological Programme and the energy crisis.

Thornton had wide interests in science and in the arts. He was especially interested in archaeology and in palaeontology and had the distinction of discovering a new species of plesiosaur (*Rhomaleosaurus thorntonii*) which can be seen at the British Museum, Natural History.

Thornton became head of the Department of Soil Microbiology in 1940. He was elected to the Fellowship of the Royal Society in 1941, of which he was Foreign Secretary from 1955–60 and a Vice-President in 1959–60. He was actively involved in the organisation of the Society's Tercentenary celebrations and was knighted in 1960. He served on the Council of the Royal Society and on many bodies concerned with microbiology and with agriculture.

Thornton was a quiet, modest man, invariably considerate and courteous with a charm of manner rarely seen today. His colleagues remember him with respect and affection.

P. S. Nutman

D. E. Wheeler

DR D. E. WHEELER who died on January 24, was a chemist who in twelve years as Managing Director of The Wellcome Foundation Limited and a further three as a Deputy Chairman was concerned particularly with the profitable translation, through development and production, of the fruits of scientific research into important drugs and vaccines. As President of the Association of the British Pharmaceutical Industry he was a leading figure during an era when regulations were being established in the wake of the thalidomide tragedy. His integrity, relied upon alike by those in industry, medicine and government, was a major

factor in the harmonious and successful negotiations. As first-ever Chairman of the Spastics Society he brought together two organisations concerned with the welfare of spastics and presided over a massive expansion on the financial side, making possible the sponsorship of original research on a considerable scale.

Denis Wheeler was born in Bristol on 6 September, 1910, and graduated from Bristol University where he specialised in physical chemistry and carried out research work which led to a Ph.D. in 1934. He was awarded a Salters' Fellowship to study industrial organisation and practice in the United States. Part of the time was spent at Princeton University where he studied advanced physical chemistry. In later years he was to become Master of the Salters' Company and concerned with the continuation of this type of scientific exchange.

On his return to Britain he joined the research department of Imperial Chemical Industries (Explosives) Ltd where he eventually became technically responsible for all acid production throughout the ICI organisation in Great Britain. In 1940 he was appointed research and development director of Hardman and Holden Ltd, chemical manufacturers.

He joined the board of directors of The Wellcome Foundation Limited in January 1946, was appointed assistant managing director later that year, joint managing director in 1948, managing director in 1955 and a deputy chairman in 1967. He retired from the board for health reasons in 1970. He was awarded the CBE in 1965.

In his early years with the Wellcome Foundation, Dr Wheeler was concerned with the organisation of development as a specific function, ensuring that the discoveries of the research laboratories could be produced in the appropriate formulations and on a sufficient scale to be administered to large numbers of humans or animals throughout the world. Whereas the research laboratories of Wellcome had been largely independent of the commercial company, he was able to convince the scientists that their work could still retain its integrity and its impetus whilst being guided towards the discovery of essential medicines, the sale of which would provide the resources for further research.

D. W. Adamson

announcements

Appointment

Brian J. Brinkworth, to the newly created Chair of Energy Studies at University College, Cardiff.

Meetings

4-6 May, **3rd International Congress on Ozone Technology**, Paris (International Ozone Institute, 52 rue d'Anjou, 75384 CEDEX 08, Paris).

8-12 May, **8th International Congress of the International Society of Psychoneuroendocrinology**, Atlanta, Georgia (R. P. Michael, Psychiatry, Emory University School of Medicine, Atlanta, Georgia 30322).

9-11 May, **Beltsville Symposium II: Biosystematics in Agriculture**, Beltsville (J. A. Duke, Plant Taxonomy, Room 117, Bldg 001 BARC West, USDA, Beltsville, Maryland 20705).

10 May, **Protein Production: Problems for the Agricultural Engineer**, London (E. Holden, The Institution of Agricultural Engineers, Silsoe, Bedford, UK).

17-21 May, **The Study of Macromolecules by NMR**, Grasmere (The Chemical Society, Burlington House, Piccadilly, London SW1).

18 May, **Opto-Electronics for Measurement and Control**, London (The Institute of Physics, 47 Belgrave Square, London SW1).

18 May, **Animal Health Products—Design and Evaluation**, Groton, Connecticut (D. C. Monkhouse, Pfizer Central Research, Groton, Connecticut 06340).

19-21 May, **The Evolution of Galaxies and Stellar Populations**, Yale (B. M. Tinsley, Yale University Observatory, Box 2023 Yale Station, New Haven, Connecticut 06520).

23-27 May, **2nd European Conference on Marine Technology—Safety at Sea**, London (WEMT 77, 10 Upper Belgrave Street, London SW1).

30 May-3 June, **Ferritic Steels for Fast Reactor Steam Generators**, London (British Nuclear Energy Society, The Institution of Civil Engineers, 1-7 Great George Street, London SW1).

1-3 June, **Environmental Pollutants—Animal Models and Wildlife as Monitors**, Connecticut (G. Migaki, Armed Forces Institute of Pathology, Washington, D.C. 20306).

1-3 June, **31st Annual Frequency Control Symposium**, Atlantic City (J. R. Vig, Fort Monmouth, New Jersey 07703).

7-9 June, **11th Annual Conference on Trace Substances in Environmental Health**, Columbia (D. D. Hemphill, 411 Clark Hall, University of Missouri, Columbia, Missouri 65201).

Person to Person

A new bivalve mollusc is spreading in the North Adriatic sea; it is similar to *Anadara* or *Scapharca* species except for its greater size (up to 8 cm). Each animal possesses several ml of haemoglobin rich blood. I would be grateful for any information on this topic. Photographs of the mollusc are available on request. Please write to Dr Silvio Buzzi, Felisatti 49, 48100, Ravenna, Italy.

Exchange furnished family house near Littlehampton, West Sussex for similar in Canberra, August 1977-July 1978. Pleasant neighbourhood, near shops, schools, and sea. Brighton 40 min, London 90 min. Exchange of car (Renault 4) also considered. Contact John Thornley, 5 Harsfold Road, Rustington, Littlehampton, West Sussex, UK.

There will be no charge for this service. Send items (not more than 60 words) to Marcus Dobbs at the London office. The section will include exchanges of accommodation, personal announcements and scientific queries. We reserve the right to decline material submitted. No commercial transactions.

7-9 June, **Deburring and Surface Finishing**, Chicago (Society of Manufacturing Engineers, 20501 Ford Road, Box 930, Dearborn, Michigan 48128).

18-19 June, **International Symposium on Gut Hormones**, Lausanne (S. R. Bloom, Medicine, Hammersmith Hospital, Du Cane Road, London).

19-25 June, **Inborn Error of Metabolism in Man**, Tel Aviv (O. Sperling, P.O. Box 16271, Tel Aviv, Israel).

20-25 June, **6th International Congress of Lymphology**, Prague (Secretariat: Sokolská 31, 120 26 Praha 2, Czechoslovakia).

20-22 June, **4th International Symposium on Mass Spectrometry in Biochemistry and Medicine**, Lake of Garda, Italy (A. Frigerio, Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea, 62-20157 Milan, Italy).

27-30 June, **Annual Meeting of the Genetics Society of Canada**, Manitoba (P. J. McAlpine, Genetics, Health Sciences Children's Center, 685 Bannatyne Avenue, Winnipeg, Manitoba, Canada).

27 June-1 July, **7th International Conference on Amorphous and Liquid Semiconductors**, Edinburgh (Secretariat, Centre for Industrial Consultancy and Liaison, 14 George Square, Edinburgh).

3-8 July, **3rd International Congress of Immunology**, Sydney (Secretary, P.O. Box 391, Darlinghurst, NSW 2010, Australia).

4-8 July, **Rhythmic Activity of Fish**, Stirling (J. E. Thorpe, Freshwater Fisheries Laboratory, Pitlochry, Perthshire, Scotland).

6-8 July, **Hot Electrons in Semiconductors**, Denton, Texas (D. G. Seiler, Physics, North State Texas University, Denton, Texas 76203).

11-14 July, **5th International Symposium on Gas Kinetics**, Manchester (UMIST, P.O. Box 88, Manchester, UK).

11-14 July, **International Symposium on Dendrochronology**, London (Organising Secretary, National Maritime Museum, London).

11-15 July, **8th International Conference of the World Association for the Advancement of Veterinary Parasitology**, Sydney (Secretary, CSIRO McMaster Laboratory, P.M.B. No. 1, Post Office, Glebe, NSW 2037, Australia).

11-15 July, **2nd International Conference on The Organometallic and Coordination Chemistry of Germanium, Tin and Lead**, Nottingham (P. G. Harrison, Chemistry, University of Nottingham, Nottingham).

17-22 July, **International Symposium on Macromolecules**, Dublin (Macro Dublin 77, Institute for Industrial Research and Standards, Ballymun Road, Dublin 9, Ireland).